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MEDICINE'S PROCLAMATION OF FAITH

PRESIDENT'S ADDRESS

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As a man counts his years, he finds among them some that are indelibly marked by an event or experience of special significance. It is the sum total of these that give meaning to his existence. Although I am proud to claim this evening, I do so with the knowledge that it is not my own. It rightfully belongs to my colleagues who have contributed so much to American medicine and to the public good.

In taking office tonight as President of the American Medical Association, I am deeply aware of the grave responsibility that the medical profession has to the people of this nation. It is my fervent hope that we shall continue to be worthy of the faith and trust that our fellow citizens have placed in us, and I pray that I can make some small contribution to a better understanding of our mutual problems.

This country was born of faith in a future free of oppression, faith in the individual enterprise of man, faith in people, and faith in the Almighty. During the past year, as President-Elect of the Association, I have traveled many thousands of miles and have had an opportunity to observe at first hand the miracle that this faith has created in our land. It is apparent everywhere that our strength and our real wealth lie in the faith of our people, for whose health we are responsible.

Sometimes I feel that physicians have been too casual in seeking public understanding. We are so interested in our work that we often fail to take the public into our confidence. We must tell the public frankly what we are doing or we cannot hope to maintain the public's confidence. Not so long ago, a friend in my home town of Erie complained to me about her inability to get a doctor at night. I asked her if she had tried to get one through the Erie County Medical Society's emergency call service. She replied she had never heard of it. I knew that we had made every effort to acquaint the public with this service, but apparently it was not enough. My friend was amazed that she could get a doctor on short notice through this service.

Similar misunderstandings have arisen about the American Medical Association because we have failed to inform the public of our objectives in behalf of the American people. Most complaints brought to our attention are the result of failure to adequately explain medical costs. The relationship between physicians and their patients would be greatly improved if doctors would anticipate this question and discuss it frankly with their patients. I also think that much of our trouble comes from the fact that our medical schools have concentrated on the scientific aspects of medicine, which is all important to the public. However, the school should also emphasize the teaching of the humanities, which, after all, is treating your brother as you would be treated yourself.

We must be trained to take into the sick room more than our scientific skill. We must allay fear, inspire confidence, and strengthen the patient's determination to get well. Unless we are willing to give of ourselves and our faith, our science will avail us little. Let me tell you of a personal experience that I believe was the best medicine I ever practiced. Several years ago I was called to care for an elderly lady who had an inoperable cancer. All we could do was make her as comfortable as possible. One morning she called me to her bedside at the hospital and asked if I would pray for her. I knelt by her bed and said the prayers while she made the responses. When I finished I ordered the nurses on each shift to take a few minutes to say prayers with the dying woman. To my amazement this sweet old lady, who lived for about six weeks, never again asked for sedatives to ease her pain. When I asked her about this one day, she replied, "Doctor Hess, I want my mind clear when these dear women pray with me."

Sometimes what we need most in the sickroom is not the medicine that we prescribe. It is the faith and the hope that we can instill in our patients. I don't care whether you are a Catholic, a Protestant, or a Jew just so long as you believe in a Power greater than all the instruments of science at your command. Faith is more than the acceptance of a creed, the practice of a religion, or the reading of a Bible. It is best expressed in that which we do every waking moment of our lives without expectation of material reward. True faith cannot be built upon a foundation of complete selfishness.

I think one of the finest examples of this type of faith has been demonstrated by the behavior of the modest, young research physician at the University of Pittsburgh

Read before the 104th Annual Meeting of the American Medical Association, Atlantic City, N. J., June 7, 1955.

—Jonas Salk. The poliomyelitis vaccine that he developed could have made him a multimillionaire, but following the tradition of Pasteur, Jenner, Banting, Fleming, and all other great medical scientists, he has repeatedly spurned monetary reward for this great work. Dr. Salk gave the vaccine to the world. He did not seek to exact financial tribute for the countless hours he spent away from his home and his family in conducting his research. Thousands of physicians voluntarily contributed their time last year in the crucial tests to check the efficiency of the vaccine. Since the results of the tests were made known this year, private physicians have again given of their time and services to administer the vaccine to first and second grade school children, who have been designated as the most susceptible to poliomyelitis. I would like to appeal to the adult population at this time to stand aside and wait for our children to get the inoculations. The children must be given this protection first, and the physicians of the nation are pledged to see that no child is deprived of the vaccine.

PROGRAM

All that the medical profession has done and will do during the years ahead is based on selfless dedication to humanity. Through the American Medical Association, the nation's physicians are united in a vigorous program to improve the quality of care in our mental hospitals, to provide adequate hospitalization and medical care for the people who cannot afford to buy insurance against the eventuality of serious illness, to encourage the building of low-cost convalescent facilities for those who suffer from long-term illnesses, and to maintain the high standard of medical education while increasing the output of physicians and the building of more medical training facilities.

Mental illness cannot be cured by buildings alone. Too many of our institutions are little more than storage places where men and women suffering from disturbances of the mind are set aside indefinitely with little hope for cure. There is a crying need for more trained help, more research, and more interest on the part of state and county governments and the public in financing adequate care for these unfortunates. More than half of the nation's hospital beds are today occupied by mental patients. Properly treated, many of these people are salvageable. The situation is critical and cannot be ignored. The American Medical Association has pledged its combined resources to solve this problem.

We know that there are many people in this country who, because of low incomes or no incomes, are unable to buy hospital and medical care insurance. Many of these individuals are in the older age groups and live on small pensions. They are the responsibility of all citizens as taxpayers in their respective communities. We doctors must do all we can, through our local medical societies, to encourage the provision of adequate hospital care for these people in their home communities and continue our tradition of providing free medical care for those unable to pay. We need more nursing homes to care for the individuals who suffer from long-term illnesses. These are the people who need hospital beds but not the expensive, specialized attention that is given patients with an acute illness. Those who suffer from a chronic illness cannot afford regular hospitalization. We are solidly behind the efforts of the federal government to help local governments build nursing homes adjacent to our hospitals that would care for the chronically ill at a nominal cost.

Now, for a moment, let us look at medical education. While the population of the nation has approximately doubled since 1910, enrollment in approved schools of medicine has increased more than 125%—from 12,500 to 28,200 students. In 1910 there were only 3,165 physicians graduated from approved medical schools, as compared to 6,861 in 1954, an increase of 115%. Within the next five years there will be 10 new four-year medical schools in operation, bringing the nation's total to 90. This will increase the number of graduates from approved medical schools to about 7,500 each year. Physicians graduating from medical schools in the United States today not only exceed in number those graduated in the early part of this century, but they have infinitely superior medical knowledge because of the high standards of medical education that have been achieved. This improvement is due primarily to the frequently misunderstood efforts of the American Medical Association and the Association of American Medical Colleges to elevate the standards of instruction in our medical schools. We have never believed in sacrificing quality for quantity and we do not believe so today.

STRENGTHENING FAITH

I have enumerated but a few of the positive steps that the medical profession is taking to keep faith with our people. We solicit your continued faith and confidence in us. At the same time, there are other areas in which the American people must strengthen their faith. Faith in our present system of government is just as important as the faith we have in ourselves and in our God. In the past 179 years, other governments have survived; ours has achieved. We have grown and we are still growing. We have progressed and we are on the threshold of even greater progress. We will never be perfect, but we are a vigorous nation, inhabited by a people gifted with initiative, imagination, and ingenuity. We must, as a people, cherish these attributes and strengthen our faith in their ability to keep our nation free. So long as we devoutly believe in the fatherhood of God and the brotherhood of man, it will be impossible to destroy America.

Faith is something bigger than we are. It is belief—belief in a Creator—if you wish, belief in God. During World War I, I served in the old Second Division. I never saw an atheist on the battlefield. The toughest prayed and swore, and even at times their profanity was a prayer. I have seen Jewish rabbis learn Protestant and Catholic prayers to aid those who were dying and Protestant and Catholic chaplains who learned the prayers of other faiths for the same reason. I have even helped a little myself in this direction when the chaplains were not around.

Yes, I am convinced that the doctor has to be a man with firm convictions concerning a Creator and be fearless in the proclamation of his faith. I care not for his creed; I care not for his race—I care much for his belief and his demonstration of that belief by his loving, tender kindness when he is called upon to alleviate human suffering.

8 E. 12th St.

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CLINICAL ASPECTS OF GLOSSOPHARYNGEAL BREATHING

REPORT OF USE BY ONE HUNDRED POSTPOLIOMYELITIC PATIENTS

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Several years ago one of the postpoliomyelitic patients at the Rancho Los Amigos Hospital was observed to be breathing in a peculiar manner, using his mouth and throat in what at first appeared to be a swallowing motion. Further observation revealed that these movements aided in breathing. With them he could breathe for many hours; otherwise he could breathe unassisted for only a few minutes. Vital capacity measurements were taken with and without the assistance of these movements and were found to be 600 ml. and 150 ml. respectively. This manner of breathing was observed in other patients, some of whom had learned it unassisted, while others had learned it from fellow patients. The first 15 cases have been reported previously.[1] The present report of 100 cases includes these 15 cases.

Because of the structures involved, we have called this procedure "glossopharyngeal breathing." It is also being called "gulping" [2] and "frog breathing," since it resembles the respiratory movements of the frog and other Amphibia.[3] We have studied the process by fluoroscopy, cinefluorography,[4] spirography, with the aid of the pneumotachograph, and airway pressure measurements, as well as by visual analysis of the patients and by self-examination of those of our personnel who have learned the technique. These observations indicate that the process consists of a pump-like action of the lips, mouth, tongue, pharynx, soft palate, and larynx (fig. 1).

Each cycle or "stroke" lasts about 0.6 second and is repeated about 10 times, resulting in an accumulation of a good-sized breath of air in the lungs. Next the accumulated breath of air is permitted to escape passively through the opened larynx. Approximately 10 such breaths are taken each minute. Figure 2 illustrates a spirogram taken during glossopharyngeal breathing by a paralyzed patient.

From the Rancho Los Amigos Respiratory Center for Poliomyelitis and the departments of Physical Medicine and Internal Medicine, College of Medical Evangelists, Los Angeles.

Read at the sixth Annual Conference on Respiratory Physiology of the National Foundation for Infantile Paralysis, Los Angeles, March 1, 1955.

The Respiratory Center is aided by an annual grant from the National Foundation for Infantile Paralysis, Inc.

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We have prepared a film describing glossopharyngeal breathing utilizing animation, cinefluorography, and patient presentation.[5] The glossopharyngeal breathing process is being studied further and will be the subject of a future report. Elsewhere we are reporting studies with regard to the effect of glossopharyngeal breathing on intratracheal and intrapleural pressures, observed simultaneously with spirograms and pneumotachograms,[6] and also on blood and alveolar chemistry.[7] The technique of glossopharyngeal breathing instruction is described in a manual that is available on request.[8]

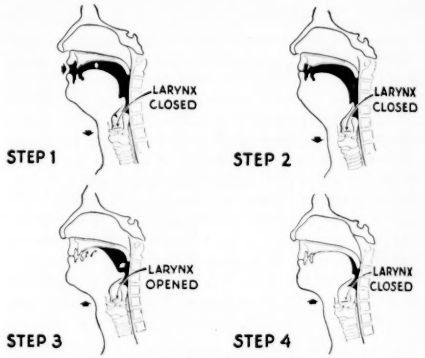

Fig. 1.—Steps taken during one "stroke" of glossopharyngeal breathing. Step 1, a mouthful and throatful of air is taken, depressing the tongue, jaw, and larynx to get maximum volume. Step 2, the lips are closed and the soft palate raised to trap the air. Step 3, the jaw, floor of mouth, and larynx are raised. This, together with progressive motion of tongue, forces air through opened larynx. Step 4, after as much air as possible is forced through the larynx, it is closed and the air is retained in the lungs until the cycle is reinitiated.

The 100 patients reported on here have all learned glossopharyngeal breathing sufficiently well to be of some practical value. All of these patients had respiratory impairment following poliomyelitis. This series represents the status of our program on Jan. 20, 1955. At that time 42 additional patients were under instruction. We considered three other patients as failures, two of these being due largely to the lack of patient initiative and one being due mainly to the lack of necessary strength. Of the 42 patients under instruction, 4 had already learned the technique but had not quite met the requirement of the series, 10 were making good progress, and 3 presented a difficult teaching problem.

METHOD OF STUDY

The criteria we have set up for this series are, first, that there is evidence of an increase in the vital capacity due to glossopharyngeal breathing, and, second, if there is

less than five minutes of ordinary breathing tolerance, that this be increased to over five minutes, the improvement in time with glossopharyngeal breathing being at least five times that without it. The patients must fall into one of the following functional groups: (*a*) patients who depend on glossopharyngeal breathing for their time breathing without respiratory equipment (depend); (*b*) patients whose spontaneous breathing is aided by glossopharyngeal breathing and who develop fatigue when using only the ordinary muscles of breathing (assist); and (*c*) patients who have appreciable time (at least one hour) free of respiratory equipment who do not use glossopharyngeal breathing except to aid in coughing and chest stretching (coughing).

The following data were tabulated on each of the 100 patients: group classification, method of learning glossopharyngeal breathing, date of onset of poliomyelitis, date of learning glossopharyngeal breathing, date of glossopharyngeal breathing evaluation, age and sex, body height, predicted normal vital capacity, observed vital capacity, vital capacity using glossopharyngeal breathing, and expiratory reserve. In the first group the following

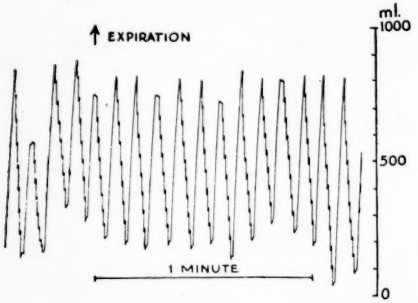

Fig. 2.—Spirogram taken during glossopharyngeal breathing by a paralyzed patient. A standard basal metabolism apparatus was used for this purpose. Note the small increments of volume change with each stroke or cycle and the large sweep during each expiration.

factors were also noted: time free of respiratory equipment when using ordinary breathing and when using glossopharyngeal breathing and the glossopharyngeal breathing stroke volume and stroke duration. The different items were averaged for each group and then were averaged for the whole series.

The predicted normal vital capacity was calculated for age, sex, and body height by the formulas of Baldwin and co-workers.[9] Vital capacity measurements were made with a Sanborn waterless spirograph (basal metabolism apparatus with low air flow resistance). The tracings thus obtained were also used in calculating the stroke volume and time period. In some cases the vital capacities and stroke volumes were determined with a simple spirometer. The expiratory reserve volume was included in the glossopharyngeal breathing vital capacity. Volumetric figures were not corrected to standard conditions. Many observations are qualitative and clinical in nature and will be described, not tabulated. The effect of glossopharyngeal breathing on blood pressure and pulse rate was observed in some of the cases. In a few instances patients were asked to blow as hard as possible into a tube connected to a calibrated aneroid pressure gauge. This we have called "expulsive force." It indicates the measure of force behind coughing.

9. Baldwin, E. de F.; Cournand, A., and Richards, D. W., Jr.: Pulmonary Insufficiency: Physiological Classification, Clinical Methods of Analysis, Standard Values in Normal Subjects, Medicine **27**: 243-278 1948.

FINDINGS

The patients learned glossopharyngeal breathing anywhere from two months to four years after the onset of poliomyelitis. This time period does not necessarily have anything to do with success of learning. In the more recent cases this period was shorter because emphasis was placed on instruction. The time required for patients to learn the technique once instruction began was not recorded in these cases. It is known, however, that some patients learned effectively in only one lesson. Others required many lessons covering a period of several months. After learning the basic technique of glossopharyngeal breathing most patients had to spend weeks of hard practice to increase strength and endurance for appreciable breathing time or for effective coughing and stretching ability. In planning for a specific patient we usually allowed about three months for learning and developing glossopharyngeal breathing. Of course, the patient must have functioning glossopharyngeal and laryngeal muscles.

Of the 100 patients, about 55 were instructed chiefly by hospital personnel, 25 learned without appreciable help from anyone, 15 learned from other patients, and 5 learned the method, not being aware of what they were doing. One of these five patients is the first one we observed. Another of these patients learned this breathing in childhood many years before he was paralyzed. He stated that he made good use of this technique to help him stay submerged in water. Another patient who had respiratory paralysis from poliomyelitis in 1933 reported that she started to breathe this way several months after the onset of her involvement. One patient was 6 years of age when first observed doing glossopharyngeal breathing, but apparently he had learned two years previously. The last of these was 14 years of age and had learned independently before evaluation.

The table enumerates some of the data that we have obtained from this study. Thirty-one patients used glossopharyngeal breathing for aid in coughing and chest stretching; they did not need it to aid in breathing. Sixty-three patients were male and only 37 female. In the group of patients who depended on glossopharyngeal breathing, however, the number was predominantly female. The sex distribution cannot be explained easily. The average age of 28 years appears to reflect our overall adult poliomyelitic population in this hospital. The youngest to learn was 4 years of age; the oldest was a man aged 47. Relatively few children learned the technique.

Increase in Breathing Tolerance.—The most remarkable finding demonstrated in these figures is the great increase in breathing tolerance that is acquired in a patient with respiratory weakness after learning glossopharyngeal breathing. On the average, the 42 patients in the

first group breathed only about a minute without artificial help using the ordinary breathing muscles; with glossopharyngeal breathing this was increased to over three hours on the average. The average vital capacity without glossopharyngeal breathing was only about 7.3% of normal. This is barely enough to maintain quiet pulmonary ventilation. A great increase in vital capacity resulted from glossopharyngeal breathing, an average of 39% of normal.

Average Findings by Groups in 100 Patients Using Glossopharyngeal Breathing

Group Classification	Depend	Assist	Coughing	All
No. of cases	42	27	31	100
Male	18	20	25	63
Female	24	7	6	37
Age, yr.	29	30	26	28
Standard vital capacity, ml.	3,510	3,920	3,900	3,760
Ability to breathe unassisted, min.	1.0	..	..	..
Ability to breathe with glossopharyngeal breathing, min.	184	..	..	..
Observed vital capacity ordinary breathing, ml.	246	666	1,270	687
Expiratory reserve volume, ml.	6	44	167	59
Percentage of normal vital capacity	7.3	18	32	18
Vital capacity using glossopharyngeal breathing, ml.	1,340	1,708	2,360	1,790
Percentage of normal vital capacity, ml.	39	49	69	47
Stroke volume	59	..	..	..
Stroke duration	0.6	..	..	..

Figure 3 illustrates a tracing of a typical adult patient who uses glossopharyngeal breathing at every breath. In the first part of the tracing he is maintaining sufficient ventilation for comfort using glossopharyngeal breathing. Note that, as in figure 2, every inspiration consists of several glossopharyngeal breathing strokes. In this tracing, however, the initial step or volume change is greater than the subsequent stroke volumes. This initial step is associated with an initial inspiratory tug by the ordinary inspiratory muscles—in this case diaphragm and neck accessory muscles. The patient who produced the tracing in figure 2 did not mix his breathing this way. The mixing of glossopharyngeal breathing with ordinary breathing at every breath is practiced quite commonly among patients and in our experience is not at all objectionable but rather desirable. Where indicated by three arrows the patient demonstrates his ordinary vital capacity, which measures 390 ml. The patient is able to breathe only a few minutes using his ordinary respiratory muscles, whereas with glossopharyngeal breathing he can breathe for three hours at a time. With a maximal glossopharyngeal breathing effort this patient can force in 2,250 ml. Since the effort of maximal glossopharyngeal breathing is associated with considerable increase in intratracheal pressure because of the increased lung volume, the patient can cough and raise tracheal mucus with much greater efficiency than when using his ordinary muscles or even with the aid of the respirator. The maximal intratracheal pressure (expulsive force) in this case measured 25 cm. H_2O after a deep glossopharyngeal breathing expansion as compared to 12 cm. with the aid of his regular respirator pressures. The section of small excursions at the end of the tracing is produced by diaphragmatic breathing. He is now able to practice from two to four minutes in this manner.

The volume of air produced by each stroke is clearly shown and measured in this type of tracing. It is our observation that effective breathing requires a stroke of at least 1% of the predicted normal vital capacity. The reported average of 59 ml. is well over this minimum figure. The speed of the recurring cycles has something to do with effectiveness of breathing. Some are able to complete each stroke in 0.3 second; some require as long as a second; the average in this series was 0.6 second.

The second group of patients who use glossopharyngeal breathing only as an aid in breathing, coughing, and chest stretching naturally have a higher ordinary vital capacity than the first group. The glossopharyngeal breathing vital capacity of 49% of normal in this group is higher than that of the first group, but the improvement in relation to ordinary vital capacity is not as great. In some of the patients in this group the benefit derived from glossopharyngeal breathing is of remarkable value in general physical rehabilitation. The third group uses glossopharyngeal breathing solely for chest stretching and coughing. Almost doubling the lung volume to 60% of normal capacity may assist in maintaining greater chest and lung compliance. By this means the force back of a cough is greatly increased also. It has been our observation that in this group there are many who are prone to develop atelectasis and pneumonia simply because of a lack of a good cough, and with glossopharyngeal breathing coughing this incidence can be decreased. Patients describe pain in the chest upon taking deep glossopharyngeal breathing inspirations and state that after practicing this stretching for a period of several weeks more expansion (as shown by increased vital capacity) can be accomplished with less pain.

Reactions and Complications.—No obvious reactions or complications that could be ascribed to glossopharyngeal breathing have been demonstrated in this series of patients. Four of this group have died of medical complications, but there appeared to be no relationship between death and this method of breathing. There have been a few patients who have swallowed air into the stomach, but this has been inconsequential. When the patient is properly instructed this does not occur. There have been some complaints of drying and irritation in the throat. This is usually overcome after several weeks

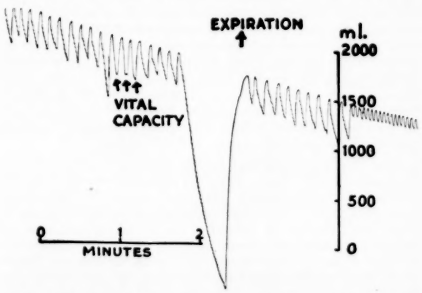

Fig. 3.—Spirogram of glossopharyngeal breathing compared with a vital capacity tracing and a tracing produced by a very weak diaphragm. There is also demonstrated a maximal glossopharyngeal effort (see text).

of practice. If the patient can learn to breathe through the nose there is less difficulty with drying and throat irritation.

When there is appreciable weakness in the muscles of swallowing and speech the learning of glossopharyngeal breathing is correspondingly difficult or impossible. It may be undesirable, therefore, to encourage such a patient in learning this technique. We have observed that if the patient has some ability to breathe unassisted he will learn more easily. If he depends on constant artificial respiration the effort to learn may be exhausting. Such a patient must have adequate general rest, and it may be undesirable to have him attempt to use new equipment or carry on with other programs while learning glossopharyngeal breathing. A strong incentive is essential to the successful learning of this method.

Arterial blood pressure and pulse rate measurements were made in nine of the patients on 32 different occasions. The patients chosen were able at the time to breathe only 1 to 10 minutes without glossopharyngeal breathing but 1 to 11 hours with it and were able to increase their breathing time at least twelvefold. Measurements were taken before and after their glossopharyngeal breathing test periods, which lasted from 20 minutes to four hours. At no time was there any abnormal blood pressure or pulse rate, nor were there any significant changes. The average blood pressure before the test periods was 109/72, mm. Hg, and afterward it was 110/71 mm. Hg. The average pulse rate before was 84, and afterward it was 89.

REPORT OF CASES

Case 1.—In a male patient who was 33 years of age at the time of this evaluation the onset of poliomyelitis was October, 1950. There was and remains paralysis of essentially all skeletal muscles except for some function in the neck and good function in the face, mouth, throat, and larynx. At the onset and for many months thereafter the use of full-time artificial respiration was mandatory. The vital capacity never went over 175 ml., about 4% of the expected normal, and this was produced by the use of neck accessory muscles. Endurance without respiratory aid was negligible until the patient learned glossopharyngeal breathing about one and one-half years after the onset of his illness. When the patient was discharged home he could breathe independently for one-half hour, and now, about a year or so later, he can breathe for two or three hours. He is able to travel in a car without a respirator. However, he is encouraged to take one along for safety. With glossopharyngeal breathing his vital capacity is 800 ml., or 19% of normal.

Case 2.—In a man, aged 36, the onset of poliomyelitis was September, 1950. There remains marked involvement of the muscles of the extremities. The vital capacity is 800 ml., or 19% of normal. The patient requires respiratory assistance at night only. During the waking hours breathing had been accomplished easily lying down, but when sitting he could breathe unassisted for a few minutes only until he learned glossopharyngeal breathing about 12 months ago. Since he has learned the technique he is able to breathe easily without tiring while sitting upright in a wheel chair for several hours. The glossopharyngeal vital capacity is 2,770 ml., or 64% of normal. His ability to sit has made possible the use of arm slings for eating. Other activities are improved also. Social contacts are much more satisfactory. With the increased reserve and coughing strength the patient can effectively clear mucus from his airway, and now needs no help by manual coughing and tracheal suctioning. In fact, his tracheal tube was removed three months ago.

Case 3.—In a male patient, 39 years of age, the onset of poliomyelitis was October, 1952. His muscles were almost completely paralyzed, the only remaining muscle function being in the face, mouth, and throat, and some weak neck muscle action. He became completely dependent on artificial respiration. About nine months after the onset of his illness he learned glossopharyngeal breathing. In six weeks he became sufficiently proficient to expand his lungs with 2,000 ml. of air. His ordinary vital capacity was 290 ml., about 7% of normal. He was discharged about a year ago using a chest-abdomen cuirass respirator, except for the time that he used glossopharyngeal breathing. Since then he has had no serious complications. His longest continuous stretch using glossopharyngeal breathing has been 14 hours. Ordinarily he does glossopharyngeal breathing for three to four hours at a time, however, since it is difficult for him to eat without artificial respiration. He has ridden in a car for distances up to 160 miles without mechanical respiratory assistance. He is able to administer his business affairs much as he did before poliomyelitis.

Case 4.—The degree to which glossopharyngeal breathing may be employed in stretching the chest is illustrated by a 32-year-old male patient. He became ill with poliomyelitis in January, 1953. This patient never required respiratory aid; however, there is appreciable weakness, especially of coughing force. His vital capacity is 3,200 ml., or 75% of predicted normal. With glossopharyngeal breathing he is able to increase his ordinary vital capacity by 2,200 ml., giving him a total of 126% of normal. Observation of the patient expanding his chest is quite remarkable, and the patient is able to make good use of his increased vital capacity in cough and expanding the chest.

Case 5.—That glossopharyngeal breathing may be of considerable assistance in talking is illustrated by a 28-year-old minister who had acute poliomyelitis in December, 1953. His natural vital capacity is 27% of normal, but he is able to raise it to 67% of normal by glossopharyngeal breathing. He finds the added volume that he gets with glossopharyngeal breathing of help in forming longer phrases of speech on one breath. This is a definite aid to him when speaking in public.

ADVANTAGES AND INDICATIONS

The advantages of glossopharyngeal breathing are many. The greatest advantage is that it is a breathing substitute requiring none of the ordinary respiratory muscles and no mechanical equipment. It provides, therefore, a built-in safety factor, important both psychologically and physically. It increases the length of time a patient can be free of equipment and supports greater physical activity such as sitting, walking, and talking. It enables the patient to cough, which in turn may prevent or minimize frequent pulmonary complications, and it also provides deeper breaths, which will help to maintain the flexibility of the thoracic structures. Any of these advantages may be sufficient reason for learning the technique. There do not appear to be any definite dangers. We consider it unsafe, however, for the patient to be left unattended if he depends largely on this breathing. The reason for this is that, should he choke, his sole mechanism of breathing may be unable to function because of spasm. Another reason for caution is the presence of a tracheotomy tube, which of course has to be plugged. It is possible that the plug or inner cannula may become loosened, leaving the patient helpless.

The patient may remark about a full sensation in the head and a feeling of faintness when taking a deep glossopharyngeal breath. Glossopharyngeal breathing, like most forms of mechanical respiration or resuscitation, is a form of positive pressure breathing. Positive pressure breathing interferes with venous return to the right side of the heart, but this appears to be compensated for by an intact circulatory system, provided the positive pressure phase is not prolonged. It is our observation that, when the patient takes breaths not greater than about one-fourth of the expected normal vital capacity, there is no appre-

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ciable effect on circulation. The few blood pressure and pulse rate measurements we made support this observation. It is our opinion that an occasional deep breath for chest stretching and coughing is not objectionable but is, in fact, desirable. When the patient is instructed to use glossopharyngeal breathing for chest stretching we advise that he take as deep a breath as possible with the regular inspiratory muscles and that, as he holds these muscles contracted, the desired stretch be accomplished by additional glossopharyngeal strokes. This will minimize the positive pressure effect and increase maximal volume change.

SUMMARY

Glossopharyngeal breathing consists essentially of pumping air into the lungs with the aid of the mouth and throat structure, instead of the use of the normal breathing muscles. Of 100 patients who used this method 69 used glossopharyngeal breathing to assist in their breathing and 31 made use of glossopharyngeal breathing in stretching the chest, coughing, and as an aid in talking. Of the 69 patients, 42 depended entirely on glossopharyngeal breathing in order to be free of artificial respiration. At the present time 42 additional patients are receiving instruction in glossopharyngeal breathing. The advantages to the patient are ability to breathe without respiratory equipment when no breathing ability exists, ability to increase breathing and activities when there is impairment of respiration, and ability to increase coughing effectiveness, as well as ability to stretch the chest structures. When it is properly directed, there appears to be no definite cause for objection to this form of breathing. On the contrary, it has been found to be of great help in aiding the return of natural breathing. With a few precautions there appear to be no dangers present in the use of this breathing technique.

Rancho Los Amigos (Dr. Dail).

HEMOLYSIS IN BLOOD COLLECTED FOR PLASMA PROCESSING

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Since the start of the National Blood Program in 1950 there has been a consistent loss of a small percentage of blood collected for processing into plasma due to excessive hemolysis. Although the over-all incidence of hemolysis has been fairly consistent, the daily occurrence has been sporadic, and not attributable to any one collection center. This recurring irregularity has aroused much curiosity and, indeed, concern, for although the percentage is small, it represents a formidable total number of units of blood. Many of these bloods are not lost entirely, for they may be diverted to fractionation. Still, the constant presence of unnecessarily hemolyzed blood of unknown cause has been a matter for consideration. Since hemolysis often results from improper techniques, such as contamination [1] or rough handling of the blood including temperature irregularities,[2] it serves as a readily available sign of trouble [3] when seen in whole blood or blood collected for plasma. Visible hemolysis represents cellular damage no matter what the cause. Improper storage temperature and bacterial contamination, common causes of hemolysis, if undected may cause sickness or death in the recipient.[4] It is, therefore, important to both recognize and appreciate the seriousness of visible hemolysis, as an aid in avoiding the transfusion of potentially dangerous blood. The study reported here was undertaken in order to determine the cause of this sporadic hemolysis, and to set forth recommendations to eliminate or at least modify it.

The term hemolysis, as applied to the field of blood banking, refers to red blood cell destruction of a magnitude great enough to impart a characteristic wine-red color to the plasma after the remaining cells have sedimented. The minimum amount of free hemoglobin visible in plasma is generally considered to be 10 mg. per 100 cc.[5] The Minimum Requirements for Normal Human Plasma, 9th revision, Laboratory of Biologics Control, National Institutes of Health, specify that plasma containing more than 25 mg. of hemoglobin per 100 ml., as estimated by gross examination, shall not be used in the preparation of processed plasma. Efforts to prevent hemolysis during the storage of whole blood have resulted in the development of successful anticoagulant solutions as well as storage conditions. The anticoagulant preservative solutions now in use are adequate to prevent visible hemolysis in blood stored over a period of 21 days.[6] Correspondingly, it has

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This study was made with the cooperation of the Laboratory of Biologics Control, National Institutes of Health, the American National Red Cross, and the Department of Defense.

The Red Cross Defense Blood Center in Kansas City, Mo., under the direction of Dr. Lorraine Sherwood, was selected for this study.

All blood for this study was processed at Armour Laboratories, Fort Worth, Texas.

The bottles for gravity collection were supplied by Sharp & Dohme, Division of Merck & Co., Inc., Philadelphia 1.

1. Whitby, L.: The Storage and Preservation of Blood and Blood Derivatives, in Brewer, H. F., and others: Blood Transfusion, Baltimore, Williams & Wilkins Company, 1949.

2. Gibson, J. G., 2nd; Sack, T.; Evans, R. D., and Peacock, W. C.: The Effect of Varying Temperatures on the Post-Transfusion Survival of Whole Blood During Depot Storage and After Transportation by Land and Air, J. Clin. Invest. **26**: 747 (July) 1947.

3. Officer, R.: Blood Storage on Active Service, Australian & New Zealand J. Surg. **12**: 111, 1942.

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5. DeGowin, E. L.: Storage and Preservation of Whole Blood, in DeGowin, E. L.; Hardin, R. C., and Alsever, J. B.: Blood Transfusion, Philadelphia, W. B. Saunders Company, 1949, pp. 306 and 314.

6. Rapoport, S.: Dimensional, Osmotic, and Chemical Changes of Erythrocytes in Stored Blood, J. Clin. Invest. **26**: 591 (July) 1947.

been demonstrated that the 4% sodium citrate solution used for the prevention of coagulation in blood collected for plasma is not harmful over the four day period of use.[7] Since all these experiments have been done with blood collected by the gravity technique, it is a reasonable assumption that hemolysis encountered using the vacuum method of collection, other things being equal, is in some way initiated by the action of the vacuum. Since hemolysis occurs only in occasional bottles, it may be assumed that the conditions causing it are variable either in their presence or in their degree of severity. The possibility that this variation may be due to differences in the fragility of donor's cells [6] is certainly a real one. However, since gravity collection does not ordinarily encounter this problem, it seems reasonable to assume that conditions of vacuum collection might be adjusted to avoid it. A critical analysis of the physical aspects of blood transmission from vein to bottle during vacuum collection clearly indicates factors that could be responsible for the violent rupture of many red blood cells, particularly if fragility was increased. It is, on the other hand, a simple matter to demonstrate that a vacuum, applied after gravity collection, does not produce hemolysis. This in itself proposed that factors concerned with collection, handling, and storage are the likely causes of hemolysis in the presence of a vacuum.

Vacuum collection has been standardized as a means of collecting blood for national defense, because it is thought to offer advantages such as ease of collection as well as reducing the possibility of air-borne contamination, as compared to the vented or the open system of blood collection.[8] The orientation of this study was therefore directed toward a better understanding of the factors concerned with the collection of blood by vacuum and the shipment of blood with residual vacuum. It was hoped that a small number of highly significant yet controllable factors might be found that could be readily eliminated, with a resulting improvement in the quality of the blood collected.

PROCEDURE

The study was made in a typical donor center under average conditions found in centers that stimulated this work. Four donor nurses drew all the blood over a period of a little more than a month. Each nurse recorded data pertinent to her collections. Two additional nurses were employed in making specific measurements on the bottles, and preparing them for use after recording their identification numbers. On each of 20 days, the technique of collection or equipment used was varied slightly and the conditions relative to each bottle recorded as accurately as possible. Conditions not being studied specifically were maintained constant throughout the study. Immediately after filling each bottle a sample of blood was taken by gravity from the donor tube. A sample was then removed immediately from the bottle by sterile syringe and needle. A third sample of blood was removed from the bottle soon after arrival at the processing plant. The plasma from these aliquots was measured for hemoglobin concentration after centrifugation, by a Coleman Jr. spectrophotometer, at a wave length of 540 mμ. This reading gave an index of hemoglobin present, thus aiding in differentiating jaundice; however, it did not allow for cloudiness. The operator was therefore obliged to observe each tube and record its general appearance. The blood was also observed for hemolysis in the bottle after centrifugation. It should be said here that entering these bottles, even using strictly sterile technique, would not be condoned if the blood was to be stored and used as whole blood, because of the ever present danger of contamination. However, in view of the fact that the plasma was to be pooled, and subsequently irradiated with ultraviolet light and then cultured, it was felt that this procedure would not endanger the recipients. Each rejected blood was cultured both as a check on technique, and to eliminate contamination as a cause of hemolysis. One, out of 133 total rejects, was found positive.

Blood was collected both in the center and on previously scheduled mobile operations. An effort was made to collect neither more nor less than 100 units of blood each day. In most instances this goal was approached. As blood was collected, it was immediately placed in preiced insulated containers of the standard Red Cross type. A recording thermometer was placed in one container in each shipment and remained in the rack with the blood until the plasma separation process was begun at the processing plant. These recorders served to indicate the temperature changes encountered as well as giving, by virtue of their delicacy, a rough estimation of the violence of vibration and bumping encountered in transportation to the processor.

The same equipment and techniques were used throughout with the exception of the changes referring to the daily studies made. Two brands of vacuum bottles were used, usually alternately by the case (12 bottles). One bottle from each case was removed and examined for volume and concentration of the anticoagulant. Except as otherwise noted, all blood was drawn in 4% sodium citrate solution, 10 ml. for each 100 ml. of blood. Donor sets had 17 gauge needles on the donor end and 15 gauge needles on the bottle end and were of the macaroni (large, 2.5 mm. bore) type and spaghetti (small, 1.25 mm. bore) type with 17 gauge needles on each end. The operating procedures were those described in the American National Red Cross Technical Manual, except where modifications were made to collect by gravity. The following techniques were used on the days indicated.

First Day: Familiarization.—The personnel selected for the study were oriented as to its importance and the procedures to be used. The methods of recording were tried and standardized during actual blood collection but with only 42 donors.

Second Day: Standardization.—A trial run was made using the full expected capacity of the group. One hundred nine donors were taken.

Third Day: Recording of Routine Blood Collection.—No changes were made in the routine of blood collection, which had been standard practice up until this time. The results of this day's work are considered typical of the techniques now in use.

7. Strumia, M. M., and McGraw, J. J., Jr.: Blood and Plasma Transfusions, Philadelphia, F. A. Davis Company, 1949, p. 205.

8. Kendrick, D. B., Jr.; Elliott, J.; Reichel, J., Jr., and Vaubel, E. K.: Supply of Preserved Blood to European Theater of Operations, Bull. U. S. Army M. Dept. 84: 66 (Jan.) 1945.

Fourth Day: Overfilling.—All bottles were filled as full as possible, the average volume collected being 626 ml. of blood, rather than 500 ml.

Fifth Day: Underfilling.—Four hundred milliliters of blood was the goal (since that is the minimum amount permitted in a 500 ml. bottle by the National Institutes of Health to be used for conversion to plasma) but an average of 439 ml. was taken.

Sixth Day: Alcohol vs. Iodine as Stopper Decontaminant.—Alternately alcohol and iodine were used to cleanse the stoppers of bottles, and the residue was not removed in order to determine the effect of migration into the bottles.

Seventh Day: Decreased Vacuum.—The vacuum in each of the bottles was adjusted to approximate 25.25 in. Hg, as measured by a mercury manometer.

Eighth Day: Slow Start, Fast First 150 Ml.—The first few milliliters were collected slowly, after which the speed of collection was rapidly increased so that the first 150 ml. was collected rapidly.

Ninth Day: Slow Start, Slow First 150 Ml.—The collection on the ninth day was made as on the eighth day, except that the first 150 ml. was collected slowly.

Tenth Day: Vacuum Relieved After Collection.—Immediately after collection through macaroni (about 3 mm. bore and 60 cm. length, with 17 gauge donor needle) doner sets and using the same technique as on the third day, the vacuum remaining in the bottle was relieved using a sterile airway with a filter.

Eleventh Day: Increased Vacuum.—The vacuum in each bottle was adjusted to 28.375 in. Hg, as measured by a mercury manometer.

Twelfth Day: Explosive Starts.—As soon as the needle was well located in the vein, the macaroni donor tube clamp was removed suddenly permitting the blood to spurt into the bottle.

Thirteenth Day: Gravity Collection.—The vacuum collection bottles were used, but the vacuum was first released through a filter, and macaroni donor sets with 15 gauge needles were used.

Fourteenth Day: Spaghetti (Small Bore) Donor Sets, Fast Starts.—Small diameter (about 1.25 mm. bore and 55 cm. in length, with 17 gauge needles) donor sets were used with fast starts and fast bleeding.

Fifteenth Day: Gravity Collection, "Horse Bottles."—Bleeding bottles, with attached rubber donor tubing, 15 gauge needle and airway, of the type used during the World War II blood program (so-called horse bottle) were used for gravity collection.

Sixteenth Day: Spaghetti (Small Bore) Donor Sets, Slow Starts.—Small diameter donor sets were used with slow starts and fast bleeding.

Seventeenth Day: Gravity Collection.—The vacuum collection bottles were used, but the vacuum was first released through a bacterial filter. Donor sets with 15 gauge needles, coated with tris (2-hydroxyethyl) dodecylamine,[9] were used.

Eighteenth Day: Acid Citrate Dextrose Solution, Spaghetti Donor Sets, Slow Starts.—Acid citrate dextrose solution, formula "B," in vacuum bottles, was used with small bore donor sets.

Nineteenth Day: Acid Citrate Dextrose Solution, Macaroni Donor Sets, Fast Starts.—Acid citrate dextrose solution, formula "B," in vacuum bottles was used with large bore donor sets.

Twentieth Day: Slow Starts, Good Phlebotomies, Overfilling.—With standard equipment, an effort was made to eliminate hemolysis by using methods that had been found to show improvement. Although the over-all collection time might be short, care was taken to draw the first 20 to 50 ml. slowly. Emphasis was placed on careful, clean phlebotomies with use of a 5 in.-wide sphygmomanometer cuff inflated to 60 mm. Hg as a tourniquet. Bottles were not filled to the top but were overfilled rather than underfilled.

RESULTS

The results of this study clearly indicate that no single factor is responsible for the hemolysis found in vacuum-collected blood. Under ideal conditions, vacuum alone is not the cause. However, it is evident that the presence of a vacuum plus other factors may cause a serious percentage of hemolyzed blood. In this study 1,462 bottles were drawn by vacuum and 261 by gravity. Of the 1,462 bottles drawn by vacuum, the blood in 77 (5.2%) was hemolyzed enough to be rejected for plasma manufacture. The plasma in many other bottles showed a questionable pink tinge, visible, yet not dense enough to cause rejection. Of the 261 bottles drawn by gravity, none of the blood was rejected for hemolysis. That conditions of collection are important in producing hemolysis is demonstrated by the results obtained by starting the blood through large bore donor tubes "explosively." The needle was inserted well into the vein, and the donor tube clamp was removed suddenly permitting the blood to race through the tube and explode into the bottle. Of a total of 104 bottles handled this way, the blood in 14.4% (15) was hemolyzed as compared with the hemolysis rate of 4.1% found on the day of routine collection (third). When the first few milliliters were started slowly but the over-all speed for the first 150 ml. was rapid the percentage hemolyzed dropped to 9.7% (8 out of 82). Of 106 units, 6 (5.6%) were hemolyzed when the blood was started slowly and regulated throughout collection. It is interesting that blood collected in acid citrate dextrose solution also showed an increased rate of 8.4% hemolyzed when the start of collection was rapid as compared with 4.6% when slow. When the collection of blood was slowed by the use of the spaghetti or small lumen donor sets, the results were markedly improved, even though an effort was made to start the blood rapidly. Of 86 units started rapidly, the blood in none was hemolyzed. Of 97 units started slowly using these sets the blood in 3 (2.8%) showed hemolysis. The increased resistance imparted by the small tube apparently retards the flow of blood preventing damage that occurs from explosive starts or rapid collection. The use of this small lumen tubing (approximately 1.25 mm.) with its built-in safety valve in the form of friction is a practical method of regulating the rate of collection. Attempts to open a clamp or remove

9. Walter, C. W.; Murphy, W. P., Jr.; Jessiman, A. G., and Ahara, R. M.: The Retardation of Clotting of Whole Blood on Contact with Stainless Steel, Surgical Forum, Philadelphia, W. B. Saunders Company, 1951, p. 289.

a hemostat slowly on larger tubes often escape the necessary care thus permitting unintentional "explosive" starts and resulting damage.

The degree of evacuation of the bottle seems to make little difference in resulting hemolysis. It has been suggested that a greater vacuum would cause more cellular damage. As judged from the hemolysis produced in this study such is not the case. In fact, the day on which the higher vacuum of 28.375 in. Hg was used produced 2.6% hemolysis, while a vacuum of 25.25 in. Hg (just enough to obtain 500 ml. of blood in the bottle being used) produced a rate of 5.7%. A comparison of all blood collected in the study (since the vacuum was measured in every bottle before use) did not, however, substantiate this relationship of low vacuum with high hemolysis rate (table 1). Nor did it suggest the contrary as being the case. Within the limits of vacuum measured and used, no preponderance of hemolysis was found in either high or low vacuum, although the most extreme vacuum found in any number of bottles was equal to 27.875 in. Hg. The degree of evacuation, if adequate to collect 500 ml. of blood and if it does not exceed about 28 in. Hg, is therefore of little importance. This then, rules out the possibility that a moderate decrease of vacuum may eliminate hemolysis.

TABLE 1.—*Rejection for Hemolysis* Found Under Various Conditions of Blood Collection*

Condition of Collection	Total No. Bloods	Hemolysis Total No.	Hemolysis %
Vacuum (all collections)	1,462	77	5.2
Explosive starts	104	15	14.4
Fast 1st 150 ml.	82	8	9.7
Slow 1st 150 ml.	106	6	5.6
Acid citrate dextrose solution			
Fast 1st 150 ml.	59	5	8.4
Slow 1st 150 ml.	64	3	4.6
Spaghetti sets fast	86	0	0
Spaghetti sets slow	97	3	2.8
High vacuum, 28.375 in. Hg	75	2	2.6
Low vacuum, 25.25 in. Hg	63	3	4.7
Overfilled, single day	66	1	1.5
Overfilled, total	123	1	0.8
Underfilled	102	9	8.8
Vacuum released after collection	98	4	4.0
Gravity	261	0	0
Nurses (in order of considered ability)			
No. 1	494	31	6.8
No. 2	291	17	6.4
No. 3	466	21	4.8
No. 4	394	11	2.9
Hour of blood collection			
1st	214	13	6.0
2nd	306	18	5.8
3rd	278	15	5.3
4th	167	11	6.5
5th	152	7	4.6
6th	207	10	4.8
7th	236	5	2.1
8th	121	2	1.6
Phlebotomy			
Immediate	1,625	74	4.5
Slow	43	5	11.6
Delayed	19	2	10.5
"Bubbles" in donor tube			
None	1,247	49	3.9
Few	370	24	6.4
Many	67	8	11.9

* Plasma contained more than 25 mg. of hemoglobin per 100 ml.

Early in this study, before the nurses had been instructed in changes in collection technique, 66 bottles were drawn with as much blood as they would hold (table 2). The blood in only 1.5% (one) was found to be hemolyzed. Underfilling, on the other hand, caused 8.8% rejections (9 out of 102 units). Overfilling averaged 626 ml. while underfilling averaged 439 ml. of blood. A later tabulation of all units collected showed 123 bottles with 580 ml. or more. These bottles averaged 602 ml. and of them the blood in 0.8% (one) was hemolyzed. These figures imply that filling the bottle to its top, or perhaps until the negative pressure is relieved, is effective in diminishing cellular damage as evidenced by visible hemolysis. This observation confirms previous reports in the literature.[10] In an underfilled bottle, the splashing of the blood without air to act as a mechanical buffer probably results in broken cells. If the bottle is suddenly shaken, the blood readily bounds from one side to the other, stopping short as it encounters the far side of the container. This shock is probably the cause of cellular rupture, for if elicited a dozen or more times by rapping firmly on the stopper and eliciting a water-hammer click each time, most blood collected by vacuum can be damaged. The blood in 9 of 10 bottles handled experimentally in this fashion was hemolyzed. The blood in underfilled bottles under vacuum is therefore susceptible to hemolysis in handling or in shipment. Although the release of the vacuum after collection may be effective in preventing hemolysis during shipment, it introduces another step in the collection procedure, as well as the possibility of contamination. In practice it lowered the hemolysis rate slightly to 4% (4 of 98). It is recommended instead, that the use of bottles that can be filled to the top will be instrumental in diminishing hemolysis.

TABLE 2.—*Bloods Rejected for Hemolysis* Found in Each Day of Collection*

Day	Technique	%
1	Familiarization	4.7
2	Standardization	2.7
3	Recording of routine blood collection	4.1
4	Overfilling	1.5
5	Underfilling	8.8
6	Alcohol vs. iodine as stopper decontaminant	6.7
7	Decreased vacuum	4.7
8	Slow start, fast 1st 150 ml.	9.7
9	Slow start, slow 1st 150 ml.	5.6
10	Vacuum relieved after collection	4.0
11	Increased vacuum	2.6
12	Explosive starts	14.4
13	Gravity collection	0
14	Spaghetti donor sets, fast starts	0
15	Gravity collection	0
16	Spaghetti donor sets, slow starts	2.8
17	Gravity collection	0
18	Acid citrate dextrose solution, spaghetti donor sets, slow starts	4.6
19	Acid citrate dextrose solution, macaroni donor sets, fast starts	8.4
20	Slow starts, good phlebotomies, overfilling	2.0

* Plasma contained more than 25 mg. of hemoglobin per 100 ml.

Final analysis of all the information collected during this study brought to light several facts of more than casual interest. Efforts have been made on previous occasions to determine the role that any one donor nurse may have in the causation of hemolysis. In tabulating

10. Bushby, S. R. M.; Kekwick, A.; Marriott, H. L., and Whitby, L. E. H.: Survival of Stored Red Cells After Transfusion, Lancet **239**: 414 (Oct.) 1940. DeGowin, E. L., and Hardin, R. C.: A Plan for Collection, Transportation and Administration of Whole Blood and of Plasma in Warfare, War Med. **1**: 326 (May) 1941.

these data the nurses concerned were listed in order of their expected proficiency (table 1). In retrospect this proficiency was based on their enthusiasm and apparent ability in the donor room, the lowest being the one that asked the fewest questions, and incidentally asked for the least help. It was therefore a surprise to learn that their rates of hemolysis were exactly opposite from their "rated" ability. The nurse expected to have the lowest rate was highest at 6.8% while one rated the least adept had a rate of only 2.9%. The others were between in similar order. Furthermore, the greatest amount of hemolysis (6.0%) occurred during the first hour of the average blood collection day, and progressively diminished until it reached 2.1% in the seventh hour and 1.6% in the eighth hour of the blood collection day. Reason would suggest that the nurses would be more proficient when they were fresh rather than when fatigued. On the other hand perhaps fatigue made them of necessity more deliberate and therefore efficient. In the interests of economy, one of the goals of an efficient donor room is the collection of as many units of blood as possible by each nurse. This burden of speed on the nurse would seem to be a false economy since it apparently increases the rate of hemolysis.

In collecting the data, the quality of the phlebotomy was classified as immediate, slow (several thrusts), and delayed (much manipulation). Of the immediate phlebotomies, 4.5% of the blood resulted in hemolysis, while the blood in 11.6 and 10.5% of the slow and delayed phlebotomies, respectively, was hemolyzed. Slow and delayed phlebotomies did not necessarily result in underfilling.

The significance of each of these factors, namely the nurse, the hour of the day, and the expertness of phlebotomy, is difficult to evaluate. That they are important is likely, but why they are factors in the causation of hemolysis is speculative. Since the application of all the principles mentioned above does not result in freedom from hemolysis, there are factors as yet not understood. Of 100 bottles drawn using careful phlebotomies, slow starts, and overfilling (average 541 ml.), the blood in two bottles (2%) was hemolyzed. As yet uninvestigated is the relation of the donor needle to the vein. The positioning of the needle plus the availability of blood are of importance. During this study it was observed that unsatisfactory collections were frequently the result of a collapsed vein either because the tourniquet was too loose or too tight. This inefficiency resulted both from poor understanding of the hydraulics of the vascular system and because the signs of a properly applied tourniquet were not appreciated by the workers. For best results, the tourniquet should be applied on the lower third of the upper arm and should be inflated to a pressure higher than venous pressure and lower than arterial pressure. Comfort is a factor in preventing reactions and should therefore be considered in applying the tourniquet. The tourniquet should be fairly wide and smooth and should be expanded to a pressure just above venous pressure; 60 mm. Hg is usually adequate. A higher pressure produces discomfort with no increase of efficiency. Of equal importance is the position of the needle in the donor vein. In order to obtain the ideal situation in which the needle opening lies free in the vein without touching any wall, the cannula must be inserted parallel to the vein in all planes, and it must not be fixed with tape in an angulated position. Certainly there are varying degrees of misadventure in this regard, but the extreme condition would seem to be a likely cause of cellular damage. The high pressure, high velocity orifices produced when the vein collapses on a needle connected to a low pressure chamber is a probable source of damage.

The "air bubbles" seen in the donor tube are a fairly accurate index of restrictions of flow through the donor needle. These air bubbles are actually spaces separated in the column of blood by exertion of the vacuum in the bottle against a restriction of flow through the donor needle. They disappear when the restriction is removed. The presence of "bubbles" indicates a poor flow from the donor's veins and therefore likely high velocity orifices. The presence of these bubbles in the donor tube was recorded by the nurses as none, few, or many (table 1). Although this is a summation of all experiments, the marked tendency to hemolysis is easily recognizable as the apparent restriction is increased at the needle tip. The prevention of this problem encountered in vacuum collection lies in the realm of education. A better understanding of the vascular system dynamics plus intelligent use of proper equipment is necessary. The friction introduced by the use of spaghetti size donor sets is advantageous in reducing the speed of blood flow to more nearly that which can be handled through the orifice between needle tip and vein. A carefully regulated clamp may have a similar effect on larger tubing. The importance of a properly applied and inflated tourniquet cannot be overemphasized for providing both adequate blood volume and venous distention for placement of the needle.

Also investigated but found to be of no apparent significance were such factors as the volume of the anticoagulant within commercial limits; the presence of iodine or alcohol on the bottle stopper; the time from collection to icing; the donor's age, race, and sex; donor reactions; blood group and type; the time from collection to separation; the room temperature during collection; the barometric pressure; and the concentration of sodium citrate as measured in one bottle per case.

The merits of both vacuum and gravity collection are well known and need not be taken up here. However, understanding and skill are necessary for the collection of undamaged blood by either technique. For instance, in gravity collection skill in placing the needle is important in order to collect a full unit of blood without retardation of flow due to a clot in the needle lumen. In vacuum collection the vacuum in the bottle helps the blood along, resulting in full bottles with less care necessary in the placement of the donor needle. However, in so collecting, hemolysis may be caused by one or a number of the factors discussed above. Several often repeated comparisons between vacuum and gravity collection are disproved by incidental information gained in this study. For example, none of the nurses employed in the donor room had ever collected by gravity, yet after only an hour of instruction they proceeded to collect a day's quota of blood in a little less time than had been necessary previously with the vacuum technique. Furthermore, the aver-

age time of collection for two days of gravity bleeding was 7.92 minutes per unit, while the average of all the vacuum bottles filled through macaroni sets was 7.96 minutes and the average of all units filled through spaghetti sets was 7.79 minutes.

SUMMARY AND CONCLUSIONS

From the beginning of the National Blood Program there has been a small number of hemolyzed bloods. This hemolysis is important not only because there was blood lost to plasma processing but because it cannot be differentiated from hemolysis due to contamination or inadequate storage temperature. Since blood affected by either of these conditions is unsuitable for plasma manufacture or may be harmful if transfused, the presence of visible hemolysis under otherwise normal conditions should be an absolute indication for discarding the blood. The constant presence of hemolysis resulting from vacuum collection of blood encourages responsible workers to ignore this important sign of trouble.

A study has been initiated to better understand the relationship of factors involved in the hemolysis caused by vacuum collection and to make corrective recommendations. The recommendations include: (1) admission of the first 150 ml. of blood into the bottle slowly, (2) use of spaghetti type (small bore) donor sets with vacuum bleeding bottles, (3) use of blood containers that when full leave a minimum of ullage, (4) prevention of vein collapse during collection by proper tourniquet regulation and careful phlebotomies, and (5) setting of daily quota of blood drawn by each nurse at a level that will prevent haste in the donor room. This study indicates that the strict adherence to these principles will reduce the occurrence of visible hemolysis using the vacuum technique of blood collection but will probably never eliminate it entirely because of the element of human error.

EFFECTS OF PREDNISONE (METICORTEN) ON MANIFESTATIONS OF RHEUMATOID ARTHRITIS

REPORT OF EARLY CLINICAL OBSERVATIONS

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Since Hench and his co-workers [1] demonstrated the action of adrenal corticosteroids and corticotropin in treatment of rheumatoid arthritis six years ago, much experience and data have been accumulated. The consensus of opinion at the present time appears to be that these hormones are of definite, yet limited, value.[2] These limitations are the result of the balance between the therapeutic response and the occurrence of undesirable side-effects. Furthermore, these hormones have not prevented continued development of the pathological process in the joints. For this reason, biochemical investigations have explored the effects of modification of the steroid molecule aimed at enhancement of its therapeutic ratio. Prednisone, formerly known as metacortandracin, represents an outgrowth of such investigations. This steroid, recently synthesized by Schering, is produced by dehydrogenation at positions one and two of the cortisone nucleus. It is Δ 1,4-pregnadiene-17α,21-diol-3,11,20-trione. Its structure compared with that of cortisone and hydrocortisone is shown in figure 1.

Bunim and co-workers [3] recently reported on the therapeutic and metabolic effects of prednisone on seven patients with rheumatoid arthritis. They indicated that in the treatment of rheumatoid arthritis these drugs were capable of producing a greater antirheumatic response, with fewer side-effects, than the adrenal steroids hitherto available. Prednisone was made available to us for clinical study in November, 1954. Our investigation focused principally upon the response of rheumatoid arthritis to treatment with prednisone as observed in clinical practice with office and hospitalized patients. This is a report of our findings in 20 such patients treated with prednisone between December, 1954, and March, 1955.

METHODS AND CLINICAL MATERIAL

Twenty patients were treated with prednisone for periods ranging from two weeks to three months. The patients were not chosen at random. They were selected to represent one or more of the following categories: (1) patients with far-advanced, severe, but potentially reversible rheumatoid arthritis; (2) patients whose antirheumatic response to other steroids was satisfactory but in whom severe side-effects developed; (3) patients who did not achieve satisfactory antirheumatic response to other steroids in the usual therapeutic dosage range; and (4) patients with early, unequivocal rheumatoid arthritis, in whom early functional rehabilitation was a pressing necessity. Thirteen of the patients were females and

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From the Department of Medicine, School of Medicine, University of Pittsburgh; and the St. Margaret Memorial and Montefiore Hospitals.

The prednisone used in this study was supplied as Meticorten by the Schering Corporation, Bloomfield, N. J.

1. Hench, P. S.; Kendall, E. C.; Slocumb, C. H., and Polley, H. F.: Effects of Cortisone Acetate and Pituitary ACTH on Rheumatoid Arthritis, Rheumatic Fever and Certain Other Conditions: A Study in Clinical Physiology, Arch. Int. Med. **85**: 545 (April) 1950.

2. Bunim, J. J.; Ziff, M., and McEwen, C.: Evaluation of Prolonged Cortisone Therapy, A Four Year Study, Am. J. Med. **18**: 27 (Jan.) 1955.

3. Bunim, J. J.; Pechet, M. M., and Bollet, A. J.: Studies on Metacortandralone and Metacortandracin in Rheumatoid Arthritis: Antirheumatic Potency, Metabolic Effects, and Hormonal Properties, J. A. M. A. **157**: 311 (Jan. 22) 1955.

seven, males. The ages ranged from 33 to 71 years; 17 patients were over 44 years of age. The duration of the arthritis ranged from 6 months to 19 years. In the past, most of the patients had received one or more of the usual antirheumatic medications (steroids, gold, phenylbutazone [Butazolidin], etc.). Fourteen patients were receiving either cortisone or hydrocortisone immediately prior to the administration of prednisone (see table). The stage of severity of the disease prior to the institution of prednisone was classified according to Steinbrocker and co-workers.[4] In 3 patients, the disease was classified as stage 4 (most advanced, with ankylosis); in 12, stage 3 (severe, with deformity); in 5, stage 2 (moderate, without deformity); and in none of the patients was the disease classified as stage 1 (mild).

The initial dose of prednisone ranged from 20 to 60 mg. daily, given orally in four divided doses, usually at six hour intervals. With satisfactory suppression of the rheumatic manifestations, the dose was gradually reduced

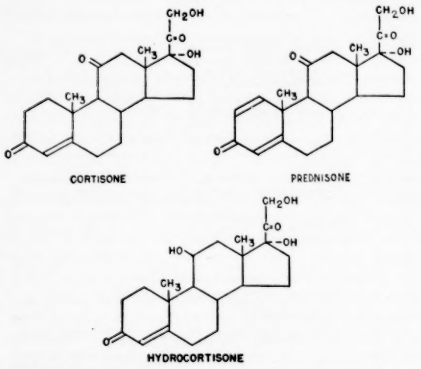

Fig. 1.—Structures of cortisone (11-dehydro-17-hydroxycorticosterone), prednisone, and hydrocortisone (17-hydroxycorticosterone).

to the smallest amount that maintained the desired therapeutic response. When too great a reduction resulted in recurrence of symptoms and signs of rheumatoid activity, the dosage was increased again to attain the desired result and daily maintenance dose of prednisone. No other antirheumatic medication was given (except for a small dose of salicylates taken voluntarily by an occasional patient). The patients were generally allowed freedom in the selection of their diet. Sodium intake was generally not restricted, and potassium salts were not administered. Physiotherapy was continued during the period of prednisone therapy. In 13 patients, therapy was begun during a period of hospitalization. The remainder were seen frequently on an outpatient basis.

Erythrocyte sedimentation rates were done by the Cutler method and read as millimeters of fall in 30 minutes. Urinalyses, determinations of the blood cell count, and concentrations of blood sugar, nonprotein nitrogen, cholesterol, and serum albumin and globulin were generally made. The results of these laboratory observations will not be reported here.

RESULTS

The response to therapy in each patient was evaluated in relation to two factors: the degree of functional impairment in each patient before and after treatment with prednisone, and the grade of response of rheumatoid activity to the drug. These were evaluated according to the criteria of Steinbrocker and co-workers.[4] The criteria for grading each of these responses are listed below.

Classification of Functional Impairment

Class 1
Complete functional capacity with ability to carry on all usual duties without handicaps

Class 2
Functional capacity adequate to conduct normal activities despite handicap of discomfort or limited mobility of one or more joints

Class 3
Functional capacity adequate to perform only few or none of the duties of usual occupation or of self-care

Class 4
Patient largely or wholly incapacitated, bedridden, or confined to wheelchair, able to perform little or no self-care

Therapeutic Criteria for Response of Rheumatoid Activity

Grade 1, Complete Remission
No systemic signs of rheumatoid activity
No signs of joint inflammation
No evidence of activity in any extra-articular process, including nodules, tenovaginitis or iritis
No remaining impairment of joint mobility, other than that associated with irreversible changes
No elevation of erythrocyte sedimentation rate

Grade 2, Major Improvement
No systemic signs of rheumatoid activity, with exception of an elevated sedimentation rate and vasomotor imbalance
Major signs of inflammation resolved, such as heat, redness of joints, and extra-articular involvement
No new rheumatoid process of intra-articular or extra-articular structures

Grade 3, Minor Improvement
Diminution of systemic signs of rheumatoid activity
Signs of joint inflammation only partially resolved
No evidence of extension of rheumatoid activity into additional articular or extra-articular structures

Grade 4, Unimprovement or Progression
Undiminished signs of rheumatoid activity regardless of functional capacity
Exacerbation of any previously involved joint or joints or development of new sites of rheumatoid activity
Roentgenologic changes indicative of progression of the rheumatoid process, excepting hypertrophic changes

It must be borne in mind that most of the patients treated with prednisone had been under our care for some time preceding the administration of this new steroid and had achieved the highest degree of improvement consistent with a safe and fully integrated program of antirheumatic management. In 14 of the 20 cases, this included the use of either cortisone or hydrocortisone in doses ranging from 12.5 to 80 mg. daily. Practical clinical considerations made it inadvisable to discontinue all previous treatment for the establishment of a base line

4. Steinbrocker, O.; Traeger, C. H., and Batterman, R. C.: Therapeutic Criteria in Rheumatoid Arthritis, J. A. M. A. **140**: 659 (June 25) 1949.

in relation to which therapeutic responsiveness with prednisone could be measured. We should emphasize, therefore, that the changes attributed to the administration of prednisone in our patients were superimposed upon those therapeutic results previously attained.

Functional Improvement.—A summary of the functional improvement is shown in figure 2. The horizontal columns represent the functional classification of each patient prior to therapy and the vertical columns, the functional classification during prednisone therapy. The dotted area above the heavy line represents the patients who showed no functional improvement. Ten patients went from class 3 functional status to a higher level. Prior to prednisone therapy, these patients were unable to work or perform their usual household chores. Following therapy, they were capable of either returning to work or caring for their household. Two patients (class 2) who were capable of working, but with much difficulty and discomfort, were relieved of this handicap and moved into class 1 after the treatment. Three patients (two of whom had structural stage 3 and one stage 4) who were largely incapacitated or confined to a wheelchair prior to prednisone therapy (class 4) were improved sufficiently by treatment to perform many of the functions of self-care and move into class 3 but were not capable of resuming their usual occupation or household duties. Five patients showed no improvement in functional classification. They did show definite increases in functional capacity; however, it was not sufficient to change their functional classification. In summary, 75% of the patients were sufficiently improved to move to a higher level of functional improvement; the remaining 25% also showed some increase in functional capacity.

Summary of Individual Patients' Response to Therapy with Prednisone

Case	Age, Yr.	Sex	Duration of Illness, Yr.	Therapy at Onset of Treatment		Status at Start of Therapy		Response		Daily Dose		Duration of Treatment, Wk.	Erythrocyte Sedimentation Rate, Mm. (Cutler-30 Min.)		Side-Effects	Remarks
				Drug*	Dose, Mg.	Stage†	Functional Class‡	Functional Class‡	Grade of Improvement	Range, Mg.	Maintenance, Mg.		Before	After		
1	57	F	4	He	80	3	4	3	2	30-25	25	4	21	5	.....	.....
2	45	F	12	He	80	3	3	2	2	60-17.5	20	12	9	2	Increased appetite, marked; moon facies, mild; insomnia; dyspepsia (gastrointestinal x-rays normal)	.....
3	47	M	½	None	..	2	3	2	2	25-17.5	25	8	22	4	.....	.....
4	59	M	22	C	62.5	4	3	3	3	40-20	20	4	15	5	Episode of gastrointestinal bleeding	Medication discontinued after 1 mo.
5	36	F	16	He	40	3	3	3	3	25-20	20	4	16	10	.....	.....
6	46	M	7	C	12.5	3	3	1	2	20	20	4	16	11	.....	.....
7	60	M	1	C	75	3	2	1	2	60-12.5	15	10	20	5	.....	.....
8	44	F	1½	C	50	3	4	3	3	60-20	30	12	22	3	Moon facies, mild; increased appetite, marked	Preexisting severe generalized osteoporosis. Hypercorticalism at start of therapy
9	71	F	19	G	2,395‡	3	3	2	2	20-15	15	12	18	4	Euphoria, mild; increase in appetite, mild	.....
10	33	F	½	None	..	2	2	2	2	60-15	17.5	10	7	2	.....	.....
11	57	F	14½	He	30	4	3	3	3	60-20	20	10	25	10	"Buffalo" type obesity, mild; hirsutism, mild	.....
12	59	F	3	P	200	3	2	1	2	20-12.5	15	10	20	9	Dyspepsia (no free hydrochloric acid on gastric analysis)	.....
13	67	F	1	He	60	2	3	2	3	40-20	20	8	3	1	Dyspepsia (gastrointestinal x-rays normal)	Hypercorticalism at start of therapy
14	56	F	8	None	..	3	3	2	2	20-15	17.5	6	17	9	.....	Previous prednisone therapy 2 mo. prior to present treatment
15	49	M	3	He	40	4	4	3	3	30-15	15	6	20	2	Increased appetite, mild	.....
16	45	F	17	He	60	3	3	2	3	30-25	30	6	16	18	.....	Hypercorticalism at start of therapy
17	66	F	14	None	..	2	3	2	2	35	35	2	19	4	Dyspepsia	Mental depression at start of therapy alleviated to moderate degree during treatment
18	48	M	7½	He	60	3	3	2	3	25-20	25	4	23	15	Dyspepsia; duodenal ulcer (diagnosed on gastrointestinal x-rays during treatment)	.....
19	55	F	6	He	60	3	3	2	3	30-25	25	4	2	2	.....	Hypercorticalism at start of therapy
20	56	M	3	He	40	2	3	3	3	30-17.5	20	6	21	5	Bigeminal rhythm	.....

* Code: He, hydrocortisone; C, cortisone; P, phenylbutazone (Butazolidin); and G, gold.
† According to Steinbrocker and co-workers.[1]
‡ Total amount to date.

Improvement in Rheumatoid Activity.—The grade of improvement in rheumatoid activity is essentially an objective evaluation. Again, it should be emphasized that the improvement in rheumatoid activity was added to that already obtained by previous treatment, which in the majority of cases included the use of other steroids.

Fifty per cent of the patients had a grade 2 objective response (major improvement) and 50% had a grade 3 objective response (minor improvement). In five patients with a grade 2 objective response, there was almost complete (grade 1) objective remission. However, literal ad-

herence to the criteria of Steinbrocker and co-workers [4] required that they be classified as grade 2. Thus, there were no patients showing a grade 1 response; neither were there any showing a grade 4 response. It is very likely that in certain instances in which a grade 2, or a nearly grade 1, remission was attained, an increase in dosage might have produced a complete remission. In the present state of our knowledge, however, it was felt that the smaller dosage produced a sufficiently adequate clinical remission to not warrant increasing the dose. Each patient felt that prednisone therapy had relieved many and, in 40% of the cases, all of the rheumatic symptoms. In every instance, there was not only the objective improvement of articular symptoms but also an improvement in the general outlook and morale of the patient.

Sixteen of the patients had an accelerated erythrocyte sedimentation rate prior to prednisone therapy; 12 of these patients had been receiving steroids. In 14 of the 16 patients, the erythrocyte sedimentation rate returned to normal during treatment with prednisone. The rapidity of this reversal was impressive.

The initial dose of prednisone was from 20 to 60 mg. daily. The maintenance dose was the least dose that would maintain the desired response observed (not necessarily maximum). Most patients could be maintained with 15 to 25 mg. of prednisone daily. While seeking the level of the maintenance dose, relapses of minimal degree were invariably noted. In such cases, the dose was increased to the maintenance level required to produce the previous remission. In a number of our patients therapy was started with seemingly low dosages of prednisone. In these, the maximum response possible from this drug was, obviously, not ascertained. In one patient (table, case 8) with severe rheumatoid arthritis, who was taking large doses of cortisone and who presented evidence of severe osteoporosis of the bones of the lower extremities prior to prednisone therapy, diminution of periarticular swelling and inflammation was achieved, but very little improvement in functional capacity was noted with prednisone.

SIDE-EFFECTS

Nine patients presented no side-effects whatsoever. Side-effects that were disturbing to the patient to varying degrees occurred nine times in seven patients. In five instances, dyspepsia developed. In one of these, it was associated on two occasions with severe epigastric distress radiating to the back. Roentgenographic study of the upper gastrointestinal tract revealed no abnormality. The distress was eventually controlled entirely by a bland type of diet and the administration of aluminum hydroxide. In one other patient who had had dyspepsia prior to administration of prednisone, a similar type of dyspepsia developed after administration of the drug, and roentgenographic study demonstrated a duodenal ulcer. In this case, there were no roentgenographic studies during previous episodes of dyspepsia occurring prior to prednisone therapy. Two additional patients, making a total of four of the five patients with dyspepsia during prednisone therapy, had had a similar type of distress at some time previous to the administration of this steroid.

One patient (table, case 4), a man with a severe, active rheumatoid arthritis and a marked anxiety neurosis of many years' standing, who had achieved a very satisfactory degree of remission after 30 days of prednisone, reported vomiting of dark brown material. He had had a history of recurrent abdominal complaints for many months prior to prednisone therapy. Under careful study in a hospital, no definite evidence of bleeding was established. Roentgenographic study demonstrated a hiatus hernia. Although this episode could not be directly related to the use of prednisone, therapy was discontinued and a relapse of the arthritis developed within one week. Administration of prednisone was later resumed, in smaller dosage, and has been well tolerated. In one instance disturbing insomnia developed during the early phase of treatment, when the initial dose of prednisone was 60 mg. It disappeared when the dosage was reduced to a level below 30 mg. In two cases, the appetite became distinctly voracious, leading to a gain in weight without clinical evidence of water retention. To summarize, there were seven patients in whom nine instances of disturbing side-effects were noted.

DURING TREATMENT

PRIOR TO TREATMENT — CLASS	1	2	3	4
1				
2	2	1		
3	1	9	4	
4			3	

Fig. 2.—Effect of prednisone therapy on functional capacity (according to Steinbrocker and co-workers [4]).

Mild side-effects occurred nine times in six patients, including moon face of mild degree in two, mild increase in appetite in two, mild insomnia in one, slight hirsutism and a buffalo hump in one, and euphoria in one. In none of these instances was the side-effect disturbing to the patient. In one patient, a bigeminal cardiac rhythm developed, which had not been noted previously.

COMMENT

The present study was undertaken to evaluate the clinical response of patients with rheumatoid arthritis to a new synthetic steroid, prednisone. The results of these short-term observations in a small group of patients with rheumatoid arthritis can serve only as a point of clinical orientation regarding the early antirheumatic effects of the drug. Our present results indicate that prednisone is a highly effective therapeutic agent capable of producing striking antirheumatic effects even when administered in smaller doses than those required with cortisone and hydrocortisone.

There is uniformly some degree of improvement in the functional capacity of the patient. In the majority of instances, the degree of improvement was strikingly apparent to the patient as well as to the observer. Objective

improvement occurred in all 20 patients; 10 showed marked improvement. There was definite amelioration of joint tenderness, heat, and swelling; and the range of motion increased. Improvement occasionally occurred even in joints that had previously been accepted as too deformed to expect any further improvement. Subjectively, the response was excellent, the pain being completely relieved or markedly diminished in all patients.

It is highly significant that the improvement noted in this group developed in addition to the fullest effect previously attained under our supervision with the administration of the generally accepted maintenance doses of cortisone and hydrocortisone. These results indicate what may reasonably be anticipated by the physician who might substitute prednisone for cortisone or hydrocortisone in a patient with rheumatoid arthritis who had previously been on a seemingly adequate regimen of treatment. The dosage of prednisone employed for each patient was relatively small, and no attempt was made to significantly increase the dosage in order to ascertain if greater improvement could be obtained with the maximum tolerated amount.

One of the most striking advantages we observed with the use of prednisone was the absence of clinical evidence of water retention. When, in the presence of edema, we deliberately substituted prednisone for hydrocortisone or cortisone, diuresis and weight loss occurred and continued in the face of an increased dietary sodium intake. This was accomplished while an adequate antirheumatic effect was maintained and the functional capacity and objective improvement were increased over and above that which had been noted previously with cortisone or hydrocortisone. In contrast to this, we were impressed with the appearance or recurrence of dyspepsia as the most frequent disturbing symptom in the course of treatment with prednisone. It should be emphasized, however, that in four of five patients in whom dyspepsia appeared, there had been a history of similar distress sometime prior to the use of this steroid. We emphasize the frequency of dyspepsia in our small group, however, because it points to the necessity for careful study regarding the relative incidence of dyspepsia or peptic ulcer in the rheumatoid population at large and that treated with prednisone and other steroids. In the individual patient treated with prednisone, it is especially important to make careful inquiry and observation regarding abnormal gastric manifestations.

No clinical evidence of potassium depletion developed. The period of observation in this study has, of course, been too short to judge whether there will be gradual loss of the maximum therapeutic response and a need for increasing the maintenance dose with continued prednisone therapy, as has been previously observed with cortisone or hydrocortisone. Up to this point, we have not explored the fullest potential of this steroid in producing a complete remission of the total rheumatoid process with its articular manifestations and then maintaining it until a permanent natural remission has had a chance to develop. Obviously, conclusions regarding the character, incidence, and severity of side-effects will not be valid until a large group of patients has been observed over an extended period.

SUMMARY AND CONCLUSIONS

Prednisone is an effective antirheumatic drug, probably the most effective therapeutic agent currently available. In our short-term study, the superiority of prednisone to cortisone and hydrocortisone as an antirheumatic agent is clearly demonstrable. When prednisone is administered in place of cortisone or hydrocortisone in patients receiving the latter steroids in therapeutic dosage, there is in every instance striking enhancement of therapeutic effect, evident by increased functional capacity and reduction of objective manifestations of joint inflammation. This was achieved, moreover, with a lower dosage of prednisone and fewer and less severe side-effects than occur with comparable amounts of the other steroids. No attempt was made to ascertain the maximum improvement possible by increasing the dose of prednisone to tolerance. With short-term therapy side-effects are few and generally minimal. The absence of clinical evidence of water retention with the dosage used was impressive. The incidence and relationship of dyspepsia to prednisone therapy should be investigated further.

No statement can be made from this short-term study regarding the persistence of the antirheumatic effect of prednisone, its effect upon the progression of the pathological processes, or the development of side-effects with prolonged therapy. It should be emphasized that, for the patient with rheumatoid arthritis, this effective therapeutic agent must be part of a total program of management, including rest, adequate diet, physiotherapy, and preventive and corrective orthopedic measures.

ADDENDUM

Since this paper was submitted, observations concerning the diabetogenic properties of prednisone suggest that this aspect of metabolism will require close scrutiny. On the other hand, the favorable effect of prednisone on the severe anemia of some patients with rheumatoid arthritis points to the need for careful study of the effect of this hormone on erythropoiesis and on possible modification of the "hemolytic" factor in this disease.

500 Penn Ave. (22) (Dr. Margolis).

The Control of Caries.—To ask children to forgo confectionery and similar cariogenic foodstuffs, which have a high prestige value, which are frequently used as rewards, which have a pleasing taste, and which provide gratification of the oral phase of development, is unrealistic so long as parents continue to eat sweets in an unrestricted manner, and so long as society refuses to provide adequate motivation—high esteem and social acclaim of a set of sound teeth. Although a handful of children have been conditioned to a diet almost completely lacking in sweets, in the absence of motivation, it is virtually impossible to teach the mass of children a new concept or to persuade them to change their food habits. Campaigns for the control of dental caries cannot use the psychological appeal which has formed the basis of practically all nutrition work. Most of the discoveries in the science of nutrition have led to drives for better human diets, with campaigns to "eat more" of this or that foodstuff. Most of these foods are delectable and have a high prestige value in our society. To eat them and to make sacrifices to give them to our children for their better health have a strong appeal to the average man and woman, which has been used directly and indirectly by health educators. The control of dental caries, through restricted and controlled sugar intake, in the absence of community pressures, has proved more than the majority of the population can accept.—F. W. Clements, M.D., The Teeth and Food, *Medical Journal of Australia*, Feb. 26, 1955.

MAJOR UNDESIRABLE SIDE-EFFECTS RESULTING FROM PREDNISOLONE AND PREDNISONE

Alfred Jay Bollet, M.D., Roger Black, M.D.
and
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Two new synthetic steroids, prednisolone and prednisone, formerly known as metacortandralone and metacortandracin, respectively, have recently been introduced as antirheumatic agents in rheumatoid arthritis.[1] They have been found to be four times more potent than cortisone in suppressing the inflammatory joint changes produced by the disease. They also cause depletion of the circulating eosinophils and significant reduction of urinary 17-ketosteroid excretion. In contrast to cortisone, administration of the new steroids is not associated with sodium and water retention or with potassium loss. Early experience with the new steroids revealed the occurrence of minor undesirable side-effects, such as facial rounding, hirsutism, diminished carbohydrate tolerance, insomnia, restlessness, weakness, transitory mental clouding, acne, increased skin pigmentation, and vague abdominal distress.

The purpose of this paper is to report three cases of major undesirable side-effects that occurred in a series of 18 successive cases of rheumatoid arthritis treated with prednisolone or prednisone. A duodenal ulcer appeared in each of the three patients. In addition, one of these patients developed a depressive psychosis. The duodenal ulcers were asymptomatic and were discovered as a result of periodic gastrointestinal x-ray examinations that were done as part of a planned study. Radiographic studies of the stomach and duodenum done immediately prior to steroid administration in two of the three patients had revealed no abnormal findings. In the third patient pretreatment x-rays were not done.

REPORT OF CASES

CASE 1.—A 67-year-old housekeeper was admitted to the Clinical Center with a 15 year history of arthritis that began with intermittent pain and swelling of several metacarpophalangeal and proximal interphalangeal joints. Involvement of the knees, ankles, and wrists ensued. Symptoms became constant and progressive, leading to almost complete disability. The only treatment she had received was aspirin, which gave slight relief. She had not previously experienced any gastrointestinal symptoms other than anorexia. Physical examination revealed a thin, weak, elderly white woman with considerable pain, stiffness, swelling, and tenderness of most peripheral joints; effusions in both knees; and generalized adenopathy. Laboratory examination disclosed a moderately severe anemia, with a hematocrit of 31%. The sedimentation rate was 120 mm. per hour (Westergren). The serum contained C-reactive protein (4+); the serum albumin concentration was 1.8 and globulin 4.5 gm. per 100 cc. X-rays of the joints presented evidence of cartilage destruction, osteoporosis, and cystic areas of subchondral bone destruction.

The patient was treated in the hospital with 4.5 gm. of aspirin daily for four successive months. Only slight improvement in symptoms or joint findings occurred, although mild symptoms of salicylate toxicity developed. After a period of placebo administration, prednisolone was given orally in daily doses of 35 mg. Marked subjective and objective improvement occurred within 48 hours. The sedimentation rate fell to 11 mm. per hour, C-reactive protein disappeared; the serum albumin level increased to 3.7 gm. per 100 cc.; and the serum globulin level fell to 2.8 gm. per 100 cc. The hematocrit increased to 44%. This improvement persisted while the dose was lowered by 5 mg. per day at weekly intervals until a daily dose of 15 mg. was reached. After 12 days of this dosage, a partial return of joint pain and swelling occurred and the dose was raised to 20 mg. per day. Improvement again followed, and this dosage was continued for 34 days, when a further return of pain and some inflammatory joint changes, associated with a rise in the sedimentation rate to 37 mm. per hour, necessitated another increase in dosage to 25 mg. per day. The pain and objective changes subsided once again. Prednisolone was then replaced by prednisone given in the same amounts, and this dosage (25 mg. per day) was then maintained at a constant level. Slight rounding of the face, slight increase in facial hair growth, increased appetite, and transient vague pains in the legs associated with periosteal tenderness were observed during therapy with both drugs. The patient repeatedly denied having had epigastric pain or discomfort at any time.

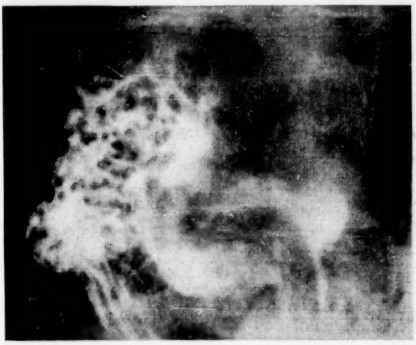

Fig. 1.—X-ray taken of patient in case 1 after 10 weeks of prednisolone therapy, showing deformed duodenal bulb with crater (arrow).

Radiological study of the gastrointestinal tract was done at the end of the 10th week of prednisolone administration, after the patient had received an aggregate of 1.9 gm. The duodenal bulb appeared deformed and presented a spastic area of contraction along the lesser curvature. A shallow ulcer crater was present near the midportion of the bulb (fig. 1). The patient was then given frequent doses of aluminum hydroxide gel and a bland diet. Steroid therapy was continued in the same dosage. Careful examination and questioning persistently failed to reveal any gastrointestinal symptoms. One month later, radiological examination was repeated and disclosed a change in the appearance of the duodenal bulb. The deformity along the lesser curvature had disappeared. Mucosal folds were now seen radiating

From the National Institute of Arthritis and Metabolic Diseases, National Institutes of Health

The x-ray studies for this report were done by Dr. Theodore Hilbish.

1. (*a*) Bunim, J. J.; Pechet, M. M., and Bollet, A. J.: Studies on Metacortandralone and Metacortandracin in Rheumatoid Arthritis, J. A. M. A. **157**: 311 (Jan. 22) 1955. (*b*) Bunim, J. J.; Bollet, A. J.; Black, R., and Pechet, M.: Metabolic Effects of Metacortandralone and Metacortandracin, Tr. New York Acad. Sc., to be published.

toward the area where the ulcer crater had been, but no crater was demonstrable at this time (fig. 2). These changes were considered indicative of healing.

An elderly woman with severe rheumatoid arthritis, who had never received steroid therapy previously, responded dramatically to prednisolone and then prednisone. She had no gastrointestinal symptoms, but a routine radiological study revealed evidence of a duodenal ulcer on the 70th day of therapy, after a total of 1.9 gm. of steroid had been given. Aluminum hydroxide gel was added to the regimen without changing the dose of steroid, and one month later there was radiological evidence of healing of the ulcer.

CASE 2.—A 16-year-old Negro male was admitted to the Clinical Center with a history of rheumatoid arthritis of three years' duration. His illness began with pain and swelling of many joints and fever. Symptoms subsided after six months,

Fig. 2.—X-ray of patient in case 1 taken one month after figure 1, showing persistent deformity of bulb, with disappearance of crater but presence of mucosal folds radiating toward former site of crater.

and he was well for the following two years. A severe exacerbation occurred, involving almost all peripheral joints and causing total incapacitation. Aspirin in doses of 4.5 gm. daily gave very little relief. He never had any gastrointestinal symptoms other than anorexia. Examination revealed an acutely ill youth with evidence of weight loss; generalized glandular enlargement; and pain, stiffness, swelling, and tenderness of almost all peripheral joints. A moderately severe anemia, with a hematocrit of 33%, was present. The sedimentation rate was 100 mm. per hour (Westergren). The serum contained large amounts of C-reactive protein (4+) and an albumin concentration of 2.5 and globulin of 4.8 gm. per 100 cc. X-rays of the joints revealed only soft tissue swelling.

After a preliminary observation period with placebo tablets, the patient was given prednisolone, 30 mg. per day. Improvement was striking and immediate. Marked diminution in malaise, pain, swelling, and tenderness of the joints was observed. The sedimentation rate fell to 2 mm. per hour, the C-reactive protein disappeared from the blood, the serum albumin concentration rose to 3.1 gm. per 100 cc., and globulin concentration fell to 2.6 gm. per 100 cc. There was a marked increase in appetite. The drug was discontinued after 12 days for research purposes, and placebo tablets were again given. Relapse of the arthritis occurred in a few days. The patient was then given a course of prednisolone for 21 days in daily doses of 50 mg. Another striking response occurred, and, after discontinuation of the medication, a slow and incomplete return of the joint changes followed. During this course the patient developed an acneform eruption, which subsided after the drug was discontinued. After a steroid-free interval of three weeks, prednisone was given in daily doses of 50 mg. for an additional period of four weeks while metabolic studies were continued. Gastrointestinal x-rays done at this time again showed no abnormality. The acneform rash returned, and he developed slight rounding of the face during this treatment. When prednisone was discontinued, a mild flare of the arthritis again occurred. Steroid therapy was withheld for six weeks. Prednisone therapy was then reinstituted, this time in doses of 30 mg. daily. All signs of arthritis again disappeared. Rounding of the face recurred, but no other side-effects were apparent.

Another x-ray examination of the gastrointestinal tract, done during the end of the third week of this course, revealed a persistent indentation on the greater curvature side of the duodenal bulb, associated with irritability and rapid emptying of the bulb. Although no crater was demonstrated, it was felt that these changes, when compared with the earlier x-ray findings, indicated the presence of a duodenal ulcer. The patient had received a total of 3.09 gm. of prednisolone and prednisone in interrupted courses. Although he had not mentioned any abdominal symptoms when previously questioned, on repeated interrogation the patient stated that he had developed mild epigastric discomfort after waking in the morning during the preceding week. This was relieved by breakfast, and pain did not recur during the day or night. Mild epigastric tenderness was noted. A regimen for treatment of peptic ulcer was begun as soon as the abnormal radiographic changes appeared. This included a bland diet, with supplementary feedings, atropine, and aluminum hydroxide gel. Prednisone therapy was continued daily in doses of 30 mg. X-ray examination repeated three weeks later revealed a disappearance of the deformity of the bulb, although irritability and coarsening of the folds were noted. It was felt that this was indicative of healing.

A 16-year-old boy with rheumatoid arthritis of three years' duration was carefully studied during intermittent courses of prednisolone and prednisone, while on a metabolic balance regimen. Each course of therapy resulted in an excellent clinical response, fall in sedimentation rate, and disappearance of C-reactive protein. Interruption of steroid therapy was followed by a slow and incomplete return of articular manifestations. Gastrointestinal x-ray studies early in his course were normal, and he then had no abdominal symptoms. A second x-ray series, done after more than 3 gm. of steroid had been administered, showed evidence of a duodenal ulcer. He was treated with diet, atropine, and aluminum hydroxide gel while steroid therapy was continued, and after three weeks there was radiological evidence of healing.

CASE 3.—A 32-year-old Negro woman was readmitted to the Clinical Center with a history of pain and swelling of multiple joints for six years. Her disease had resulted in almost complete ankylosis of the wrists and flexion contractures of the elbows, with moderate disability. Treatment with gold had caused leukopenia and albuminuria, and quinacrine (Atabrine) administration was followed by an anemia. Cortisone had given considerable relief of joint symptoms in doses of 50 to 75 mg. per day but was discontinued one and a half years before this admission. Aspirin in doses of 4 gm. per day gave incomplete relief. During her first admission to the Clinical Center 18 months previously, she was observed by a staff psychiatrist, who was then studying the personality pattern of patients with

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rheumatoid arthritis. He noted dependent and passive personality traits and described a mild depression, attributed to the arthritis and to her failure to find a suitable marriage partner. The patient had never had any gastrointestinal symptoms.

Examination during the present admission revealed a thin, chronically ill Negro woman with generalized adenopathy and pain, tenderness, and swelling of multiple joints. There was warmth of the elbows, knees, and right ankle. The wrists were ankylosed. Laboratory studies revealed a hematocrit of 38%, leukopenia (3,500 white blood cells per cubic millimeter), and a sedimentation rate of 118 mm. per hour (Westergren), with a 4+ C-reactive protein test. Her serum albumin concentration was 2.2 gm. per 100 cc. and globulin concentration 5.2 gm. per 100 cc. X-rays of the joints revealed narrowing of articular spaces and cystic areas of cortical and subcortical bone destruction. Radiological examination of the gastrointestinal tract showed no abnormality, and a glucose tolerance test was normal.

On treatment with 30 mg. of prednisone per day, there was a marked reduction of pain and stiffness, with a rapid decrease in tenderness and swelling of her joints. The sedimentation rate fell to 37 mm. per hour, and the test for C-reactive protein became negative. The glucose tolerance test was repeated on the 19th day of therapy. Although it showed no change in the fasting level, the peak concentration of glucose in the blood was now 217 at 60 minutes, and the two hour level was 110 mg. per 100 cc. The corresponding values obtained prior to therapy were 139 and 83 mg. per 100 cc. (fig. 3). On the 20th day of therapy, after a total of 600 mg. of prednisone had been given, radiological examination of the gastrointestinal tract was repeated. Although the patient had not noticed abdominal symptoms, fluoroscopic examination of the duodenal bulb showed considerable coarsening of the rugal folds, with a constant deformity along the greater curvature side. Compression films demonstrated a shallow ulcer crater near the apex of the bulb (fig. 4). During the following week, the patient began having moderately severe epigastric pain, relieved by food and aluminum hydroxide gel, and epigastric tenderness was now present.

At about this time the patient became more depressed than she had been and began to mention that she was "imagining things" and having "bad dreams" but would not describe those phenomena. Within a few days the depression became quite severe, with a marked decrease in psychomotor activity and frequent crying. She complained of "fogginess of my mind," inability to concentrate and talk, and stated that she imagined people were looking at her and that she felt guilty whenever

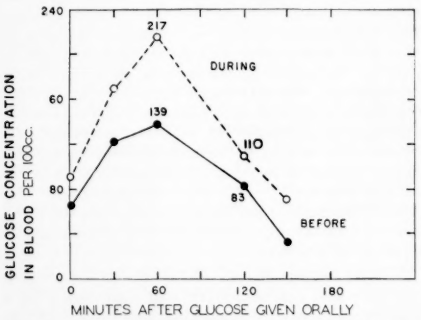


Fig. 3.—Glucose tolerance tests before and during prednisone administration in patient in case 3.

another person was near. She mentioned that she imagined she was having sexual contact with men almost constantly but knew this was not true and was distressed by this inability to control her thoughts. It was the opinion of a staff psychiatrist that the patient was having a psychotic depression. The daily dose of prednisone was reduced, and within two days it was discontinued.

There was no return of the joint symptoms or objective findings following withdrawal of steroid therapy. The psychosis, however, persisted without change, and the patient had to be under constant observation because of the frequent expression of suicidal ideas. She continued to have occasional epigastric pain, which was relieved by food or alkali and was associated with moderately severe epigastric tenderness. Radiological study was repeated eight days after the discontinuance of prednisone

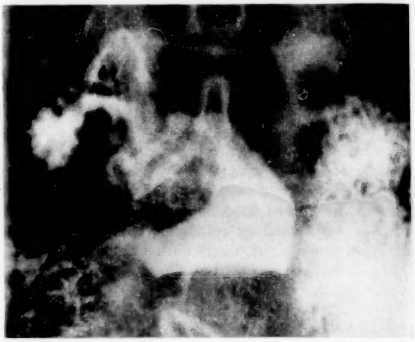


Fig. 4.—X-ray of patient in case 3 taken after 20 days of prednisone therapy, showing deformity of duodenal bulb with shallow ulcer crater (arrow) near apex.

and three weeks after the ulcer was found. The deformity of the bulb was still present, but there was less irritability and tenderness, and it was the impression of the radiologist that some healing had occurred. The patient was then transferred to a mental hospital. A report received from this hospital seven weeks after prednisone was discontinued stated that the patient remained severely depressed, seclusive, and lethargic, although she was no longer having delusions. The arthritis remained asymptomatic.

A young Negro woman with moderately severe arthritis was observed to have a chronic mild depression 18 months before prednisone was administered. Radiological study of the stomach and duodenum done prior to therapy was normal. Hormonal therapy was followed by a prompt and marked improvement of the reversible joint changes, but during the third week of medication she developed a duodenal ulcer, an abnormal glucose tolerance test, and a toxic psychosis with marked depression and suicidal ideas. Gastrointestinal x-rays taken after interruption of steroid therapy showed some evidence of improvement, but deformity of the bulb persisted. No improvement in the psychosis occurred, and transfer to a mental institution was necessary. The depression persisted, but there was no return of the joint symptoms.

COMMENT

Peptic Ulcer.—There is considerable variation in the reported incidence of peptic ulcer in patients with rheumatoid arthritis treated with cortisone or corticotropin. The incidence seems to be quite low when these drugs are given for brief periods. Sandweiss [2] found no ulcers in 65 patients, and Kuzell and Schaffarzick [3] reported

2. Sandweiss, D. J.: Effects of Adrenocorticotropic Hormone (ACTH) and of Cortisone on Peptic Ulcer: Clinical Review, Gastroenterology **27**: 604, 1954.

3. Kuzell, W. C., and Schaffarzick, R. W.: Cortisone Acetate in Thirty-Two Cases: Preliminary Clinical Observations, Stanford M. Bull. **8**: 125, 1950.

none in 17. In a series of 324 cases, Hollander [4] noted one patient with duodenal ulcer without a history of ulcer in the past, and three patients with reactivation of preexisting ulcers.

When the hormones are administered for prolonged periods, however, the incidence of peptic ulcer apparently rises (see table). In 36 of 477 cases (7.5%) reported by seven groups of investigators peptic ulcers developed. There have been several other reports in which mention is made of the appearance of peptic ulcer or of massive gastrointestinal bleeding in arthritis as well as in other conditions treated with cortisone or corticotropin. On the other hand, Bauer [5] found a 4.5% incidence of peptic ulcer in 650 patients with rheumatoid arthritis who had never received hormone treatment, and Ragan [6] reported that "about 6 to 8% have a history of an ulcer." In addition, Bauer,[5] Hench,[7] Freyberg,[8] and Hollander [4] report patients with known duodenal ulcers that were not activated or aggravated by cortisone. Many instances of healing of active peptic ulcers during cortisone administration have been reported and are reviewed by Sandweiss.[2]

Reported Incidence of Peptic Ulcer in Patients with Rheumatoid Arthritis Treated with Cortisone or Corticotropin for Prolonged Periods

Author	Total Cases	No. of Ulcers	Duration of Therapy
Bunim, J. J.: Ziff, M., and McEwen, C.: Am. J. Med. **18**: 27, 1955	71	5	6-48 mo.
Engleman, E. P., and others: Calif. Med. **80**: 369, 1954	56	2	4-38 mo.
Freyberg and others [8]	44	1	100-400 days
Copeman, W. S. C., and others: Brit. M. J. **1**: 1109, 1954	20	2	16-36 mo.
West, H. F., and Newns, G. R.: Lancet **2**: 515, 1952	6	2	21 mo.
DeMartini, F., and Ragan, C.: Personal communication to Sandweiss [2]	80	11	.....
Holbrook, W. B.: Personal communication to Sandweiss [2]	200	10	.....
Totals	477	36 (7.5%)	

In our series of 18 patients with rheumatoid arthritis treated with prednisolone or prednisone for periods of one to seven months, radiological evidence of peptic ulcer appeared in 3 patients. No patient in the series had a history of ulcer symptoms. Serial gastroduodenal x-rays were obtained at six week intervals in almost all patients receiving these steroids beginning shortly after the initiation of the study, and these periodic x-rays revealed the appearance of the ulcer in the three cases reported here. Normal gastrointestinal x-rays had been obtained earlier in two of the three patients who developed radiological evidence of peptic ulcers. Only one of these three patients had received prior treatment with cortisone or corticotropin but had not received any hormone therapy for over one year before the start of prednisone therapy. There was no apparent relationship between the duration of treatment or total dose of drug and the appearance of the ulcer.

This experience represents a greater frequency of this complication than has been witnessed in patients with rheumatoid arthritis in the past, including those treated with cortisone or corticotropin. If this incidence is substantiated by further experience with larger series of cases, it will indicate a need for added caution in the use of these drugs. It is important to note the occurrence of radiological evidence of healing of the ulcer within three weeks following institution of the usual medical, antiulcer measures, including aluminum hydroxide gel, in two patients who were maintained on an unreduced dose of the steroid. This would suggest that the prophylactic administration of an aluminum hydroxide gel concomitant with the use of these steroids might reduce the incidence of peptic ulcer.

The first indication of the appearance of a peptic ulcer in patients receiving cortisone therapy is often the sudden development of massive gastrointestinal bleeding or perforation of the ulcer and peritonitis. Although no such catastrophe occurred in our patients treated with prednisolone or prednisone, we are aware of one instance of sudden onset of massive hematemesis requiring emergency surgery one week following the end of a five week course of prednisolone therapy in a patient with nephrotic syndrome. This patient, who had no previous gastrointestinal symptoms, had been treated with cortisone before receiving the new steroid.[9]

Mental Disturbance. — Severe mental disturbances have been described in patients with adrenal cortical hyperfunction (Cushing's syndrome),[10] and the incidence of psychotic reactions induced by corticotropin or cortisone has been estimated at 5% by Glaser.[11] These reactions have been described as occurring in two general patterns: those primarily involving the affect with elation or depression, and other more complex reactions with organic features, most often associated with depression. Predisposing personality patterns are considered important, and, in most instances, determined the psychological content of the psychosis but did not seem to determine whether or not a psychosis developed.[11] No definite relationship has been established between the onset of mental symptoms and the daily or total dose of hormone administered.

The patient we observed who developed a depressive psychosis with organic features had been studied by a psychiatrist for several months one year earlier and was noted to be a depressed, dependent individual. The subsequent development of a frank depressive psychosis after three weeks of treatment with prednisone suggests that the patient's earlier personality played a prominent role in these events. As with cortisone therapy, it is advisable that patients be carefully selected for treatment with the newer steroids, giving consideration to any previous history of mental disturbance.

4. Hollander, J. L., in Proceedings of the Second Clinical ACTH Conference, vol. 2: Therapeutics, edited by J. R. Mote, New York, Blakiston Company, 1951, p. 503.

5. Bauer, W., in Proceedings of the Conference on the Effects of Cortisone, December 10, 1951, Rahway, N. J., Merck & Co., Inc., 1952, p. 56.

6. Ragan, C., in Proceedings of the Conference on the Effects of Cortisone,[5] p. 55.

7. Hench, P. S., in Proceedings of the Conference on the Effects of Cortisone,[5] p. 56.

8. Freyberg, R. H., and others: Problems of Prolonged Cortisone Treatment for Rheumatoid Arthritis: Further Investigations, J. A. M. A. **147**: 1538 (Dec. 15) 1951.

9. Pechet, M. M.: Personal communication to the authors.

10. Schlezinger, N. S., and Horwitz, W. A.: Neuropsychiatric Disorders Occurring in Cushing's Syndrome (Pituitary Basophilism), Am. J. Psychiat. **96**: 1213, 1940. Plotz, C. M.; Knowlton, A. I., and Ragan, C.: The Natural History of Cushing's Syndrome, Am. J. Med. **13**: 597, 1952.

11. Glaser, G. H.: Psychotic Reactions Induced by Corticotropin (ACTH) and Cortisone, Psychosom. Med. **15**: 280, 1953.

Alterations in Glucose Tolerance.—Alterations in glucose tolerance similar to those seen in the patient in case 3 (fig. 3) have been observed in other patients in our series who were treated with prednisolone or prednisone. These changes have been described in a previous publication.[1b]

SUMMARY

In a series of 18 patients with rheumatoid arthritis treated for as long as seven months with prednisolone or prednisone, a number of side-effects have been observed. Three patients presenting radiological evidence of peptic ulcer and one patient with severe depressive organic psychosis are reported. In the last-mentioned case definite reduction in carbohydrate tolerance was noted. The fact that the ulcers were asymptomatic in these patients indicates the need for careful observation of patients receiving these drugs in order to avoid unheralded perforation or hemorrhage. The apparent high incidence of this serious side-effect in patients receiving prednisone or prednisolone suggests the advisability of routine coadministration of an aluminum hydroxide gel. The appearance of a psychotic reaction points to the need for caution in selecting suitable patients for steroid therapy.

PUERPERAL TUBAL STERILIZATION

REPORT OF 1,830 CASES

Harry Prystowsky, M.D.
and
N. J. Eastman, M.D., Baltimore

Puerperal tubal sterilizations were performed on 1,830 women in the department of obstetrics of the Johns Hopkins Hospital between June 1, 1936, and Dec. 31, 1950. Table 1 lists the indications for sterilization; the most common were: (1) great multiparity only, 33.3%; (2) chronic hypertension and/or repeated toxemia, 17.7%; and (3) repeat cesarean section, 15.4%. As used in the clinic and in this paper, the term "great multiparity" is defined rigidly as eight or more previous viable deliveries (each fetus weighing over 1,000 gm.). The number eight was used since maternal mortality has been thought to rise sharply after the eighth delivery [1]; and, because of this fact, we have hitherto believed that great multiparity, so defined, is truly a medical indication. One-third of all the sterilizations here reported were done solely on this indication. In addition to this group, 161 women presented not only great multiparity but also had some other indication for sterilization; the most frequent was chronic hypertensive vascular disease, this combination being observed in 115 cases. The state of great parity, therefore, constituted either a sole indication or an auxiliary indication in 770 cases, or 53.8% of the total. The indication "other" refers to those cases that did not fit into the listed categories and did not constitute an indication more than five times. This group consisted of 82 cases, or 4.48% of the total. Included are patients with sickle cell anemia, neurofibromatosis (Recklinghausen's disease), dwarfism, repeated congenital anomalies in offspring, treated carcinoma of cervix uteri, bilateral macular degeneration of the retina, large hernias (umbilical, ventral, or bilateral inguinal), repeated vaginal deliveries after a previous cesarean section, colostomy, colectomy, ileostomy, thyroid diseases, rectovaginal and vesicovaginal fistulas with previous repair failures, leukemia, and previous postpartum psychosis; patients of high parity with abnormal presentations who had first cesarean sections; and patients who were deaf-mutes.

The background of the patients who were sterilized was studied in terms of race, social status, age and religion. The highest incidence was contributed by ward patients, 92.88%. This figure is undoubtedly influenced by selective screening in the outpatient department and referrals from the county clinics of Maryland. Of the ward patients, 1,076 (58.79%) were nonwhite and 624 (34%) were white. The incidence of private patients was 7.04%. A further breakdown by race and social status shows the following data: nonwhite, married, 963 cases (52.62%); white, married, 595 cases (32.51%); private, married, 128 cases (6.99%); nonwhite, unmarried, 113 cases (6.17%); white, unmarried, 29 cases (1.58%); private, unmarried, one case (0.05%); other, married, one case (0.05%); and other, unmarried, none. Of the women sterilized, 674 (36.83%) were between the ages of 20 to 29, 915 (50%) were between 30 and 39, and 170 (9.28%) were between 40 and 49. The 71 girls (3.88%) between the ages of 10 and 19 represent mainly those with grave illnesses. Most interesting was the number of patients with great multiparity in the

TABLE 1.—*Indications for Sterilization*

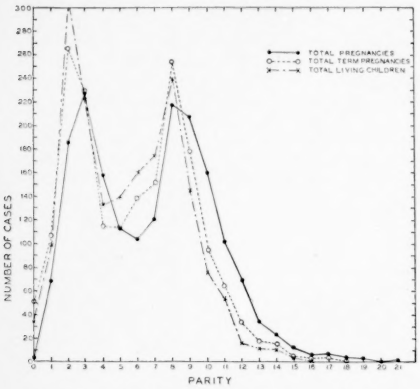
	Cases	
	No.	%
Great multiparity * only	609	33.28
Accompanying repeat cesarean sections	281	15.35
With 2nd cesarean section	11.97%	
With 3rd cesarean section	3.11%	
With 4th or more cesarean section	0.27%	
Chronic hypertension (great multiparity also in 115 cases)	238	13.00
Psychiatric	127	6.94
Heart disease	91	4.97
Repeated toxemia (great multiparity also in 28 cases)	86	4.70
Tuberculosis	68	3.72
Varicosities (great multiparity also in 18 cases)	52	2.84
Gynecologic plastic operation	36	1.97
Renal disease	35	1.91
Diabetes	38	2.07
Neurological disease	31	1.69
Epilepsy	24	1.31
Blindness	10	0.55
Other pulmonary disease	8	0.44
Disease of skeletal system	7	0.38
Rectal stricture	7	0.38
Other	82	4.48
Total	1,830	99.98

* Defined as 8 or more viable deliveries.

From the Department of Obstetrics, Johns Hopkins University and Hospital.

1. Eastman, N. J.: Hazards of Pregnancy and Labor in "Grande Multipara," New York J. Med. **40**: 1708 (Dec. 1) 1940.

lower age categories and, consequently, the very early age of child-bearing. Of the 1,830 patients, 992 (54.2%) were Protestant, 185 (10.1%) were Catholic, 21 (1.15%) were Jewish, 2 (0.11%) were of other religions, and 630 (34.42%) stated no religion. Table 2 and the figure deal in detail with parity. The 1,830 patients in this study had 12,284 total pregnancies, 10,494 full-term pregnancies, and 9,911 living children. This represents 6.7 total pregnancies per patient, 5.7 full-term pregnancies per patient, and 5.4 living children per patient. A consideration of patients with "great multiparity" shows an average of 10 pregnancies per patient. The figure shows the high incidence of sterilization with second and third pregnancies. This is attributable to sterilizations accompanying repeat cesarean sections. The next peak occurs during the eighth and ninth pregnancies and is due to great multiparity. In essence, the average patient sterilized was a married, nonwhite, ward patient between the age of 30 and 39, of Protestant denomination, who



Number of patients sterilized according to degree of parity.

had had 6.7 total pregnancies, 5.7 full-term pregnancies, and 5.4 living children.

Table 3 lists the types of operation. In 1,478 cases (80.77%), Pomeroy's operation was used; this type of sterilization was the most commonly used because it is such a simple procedure, requires but a few minutes, and causes, in our experience, a minimal number of immediate surgical complications. Since there seems to be some misunderstanding about the definition of Pomeroy's operation, it might be well to point out that it consists of ligating a loop of tube with catgut and then severing the knuckle of the loop together with the subjacent mesosalpinx. The procedure is based on absorption of the ligature and subsequent separation of the severed tubal ends, which become sealed over with a fibrinous exudate. Therefore, any technique in which a nonabsorbable suture is used, or in which the tubes and mesosalpinx are not severed, is not Pomeroy's operation. The Madlener operation for tubal sterilization is very similar to Pomeroy's in outward appearance, but is quite different in principle and in efficacy. The technique of the Madlener procedure differs in three important respects from Pomeroy's. 1. In the Madlener operation, the tube is crushed with a Kelly clamp at the site of the intended ligation; in Pomeroy's operation, it is not crushed. 2. In the Madlener procedure, silk or other nonabsorbable suture is used; in Pomeroy's, an absorbable suture is used. 3. In the Madlener operation the knuckle of the tube is not cut; in Pomeroy's operation the knuckle of the tube is cut across in such a manner that the tube stumps are completely severed. The objective of the Madlener operation is to produce occlusion of the tube by the crushing and the use of a silk suture. The aim of Pomeroy's operation is separation of the tubal ends and their occlusion by exudate.

Irving ligations were performed in 206 patients, and it may be significant that there have been no failures or serious complications with this procedure. In the earlier years the Madlener operation was frequently done; however, because of the high incidence of failures in this clinic reported by Dippel,[2] it has been discarded. The other types were done in the earlier years of the study but were not as acceptable as Pomeroy's. Most of them comprised cases in which one technique was used on one tube and another method on the other. The largest number of Pomeroy's operations were performed within a short interval after delivery. The group of 1,022 cases (referred to as puerperal sterilization) not only lends itself to statistical analysis but also represents a "pure" study of Pomeroy's operation. Four hundred Pomeroy's operations were performed accompanying cesarean section or hysterotomy. Fifty-six were performed six or more weeks post partum or in patients who had never been pregnant.

POMEROY'S OPERATION

It has been the general principle that sterilization be performed within the first 48 hours after delivery. In the earlier years, i. e., prior to 1943, longer periods of time elapsed. In table 4 it is clearly seen that 52.72% of the sterilizations were performed within 24 hours of delivery, and 23.88% on the second postpartum day. This represents a total figure of 76.6% within 48 hours. Ligations performed after the second day (23.3%) were those done in the earlier years and, to a much lesser extent, those that were performed prior to the six week postpartum deadline. The sterilizations in this study were performed by 166 interns, resident physicians, and staff members: 47.94% were done by interns, 49.5% by assistant residents and residents, and 2.54% by the full-time and visiting staff.

Anesthesia.—Thiopental (Pentothal) sodium, injected intravenously, was the most commonly used anesthetic—given to 731 patients (71.52%). The anesthetic was given by nurse anesthetists or, much more often, by members of the house staff. Its greatest use was in the patient who was hypertensive. Conduction anesthesia (14.38%) was not uncommonly used for delivery and sterilizations, thereby necessitating only one anesthetic. Local infiltration, although used in only 66 cases (6.45%), was found to be quite effectual and was frequently combined with

2. Dippel, A. L.: Tubal Sterilization by Madlener Method: Critical Analysis of Failures, Surg., Gynec. & Obst. **71**: 94 (July) 1940.

intraperitoneal application of the local anesthetic. Ether was used in 8 patients (0.78%); gas-oxygen-ether in 31 (3.03%); other inhalation in one (0.09%); and other, including combined, in 38 (3.71%). There were no anesthetic complications in 991 cases (96.96%). Of the 31 anesthetic accidents, 3 were classified as major. These were all associated with thiopental sodium and comprised severe hypotension, respiratory embarrassment, and cyanosis. Recovery was complete after proper measures were instituted, and there was no anesthetic fatality.

Duration of Operation.—Despite the high incidence of relatively untrained personnel, 91.19% of the puerperal sterilizations were performed within 60 minutes and 98.62% were done with 90 minutes. Longer operating times were secondary to both operative and anesthetic difficulties and were also present when sterilizations and incidental appendectomies were performed on patients admitted five weeks post partum.

TABLE 2.—*Parity in Patients Studied*

No. of Pregnancies per Patient	Cases		Total	No. of Full-Term Pregnancies per Patient	Cases		Total	No. of Living Children per Patient	Cases		Total
	No.	%			No.	%			No.	%	
00	3	0.16	0	00	51	2.78	0	00	34	1.85	0
01	68	3.71	68	01	107	5.84	107	01	99	5.40	99
02	186	10.16	372	02	265	14.48	530	02	310	16.93	620
03	228	12.45	684	03	225	12.29	675	03	222	12.13	666
04	158	8.63	632	04	115	6.28	460	04	133	7.26	532
05	113	6.17	565	05	114	6.22	570	05	140	7.65	700
06	104	5.68	624	06	139	7.59	834	06	161	8.79	966
07	121	6.61	847	07	153	8.36	1,071	07	175	9.56	1,225
08	218	11.91	1,744	08	255	13.93	2,040	08	240	13.11	1,920
09	208	11.36	1,872	09	169	9.23	1,521	09	146	7.97	1,314
10	161	8.79	1,601	10	94	5.13	940	10	76	4.15	760
11	102	5.57	1,122	11	65	3.55	715	11	53	2.89	583
12	69	3.77	828	12	34	1.85	408	12	16	0.87	192
13	34	1.85	442	13	17	0.92	221	13	11	0.60	133
14	23	1.25	322	14	15	0.81	210	14	10	0.54	140
15	12	0.65	180	15	5	0.27	75	15	3	0.16	45
16	7	0.38	112	16	3	0.16	48	16	1	0.05	16
17	7	0.38	119	17	3	0.16	51				
18	4	0.21	72	18	1	0.05	18				
19	3	0.16	57								
20	0	....	0								
21	1	0.05	21								
Total	1,830	99.90	12,284		1,830	99.98	10,494		1,830	99.91	9,911

Complications.—In 1,003 cases (98.11%) there was no operative complication. In the 19 cases in which complications did occur, only two were considered major; because of large, broad ligament hematomas two hysterectomies were necessary. In 48.33% of the patients there was no postoperative complication. The highest single complication was febrility (43.93%), which is defined as any temperature of 100.4 F (38 C) or above at any time during the patient's hospital stay. The most common cause of febrility by far was "operative reaction." Paralytic ileus and urinary tract difficulty were the next most common complications. Of the seven instances of wound breakdown, five were superficial, but in two complete dehiscence occurred.

Mortality.—There were three deaths, two attributable to pulmonary embolism and one to ruptured ectopic pregnancy 90 months after the operation. The mortality rate was, therefore, 0.3% in the 1,022 cases of puerperal Pomeroy sterilization. The following cases are those of the patients who died.

A nonwhite patient, who was 25 years old, para 6-0-1-6, with a normal pelvis, no toxemia, negative serologic test for syphilis whose expected date of confinement was March 8, 1943, was scheduled for puerperal tubal sterilization because of multiparity and the presence of varicosities of the labia and legs that had become progressively worse with each pregnancy and that more or less incapacitated the patient toward the end of this pregnancy. The patient was admitted on March 22, 1943, and delivered spontaneously after a total labor of 16 hours and 6 minutes. On the third day of the puerperium, Pomeroy tubal sterilization was carried out. The postoperative course, but for a low grade febrile reaction about 99 to 99.2 F (37.2 to 37.3 C) was uneventful. On the sixth postoperative day she was allowed to get up. Because of a temperature of 99.6 F that afternoon, she was put back to bed. On the next morning the temperature rose to 101 F (38.3 C) and later to 102.2 F (39 C). Fluid was found in the right pleural cavity, which was confirmed by roentgenograms. On absolute bed rest the temperature subsided to 100 F (37.8 C). On the 12th postoperative day the patient was transferred to the Medical Service, where a thoracentesis was done. A temperature between 101 and 103 F (38.3 and 38.9 C) persisted. Between 12 midnight and 3 a. m. on the 15th postoperative day, she died suddenly. The clinical diagnosis showed pleural effusion, tuberculosis of the right lung, and pulmonary embolism. At autopsy thrombosis of the vein of the right ovary was also found.

A 39-year-old woman, para 13-0-0-12, with a negative serologic test for syphilis, blood group O, Rh positive, a normal pelvis and expected date of confinement on March, 1950, was referred from Prince Frederick County, Maryland, for delivery and postpartum tubal ligation. The patient delivered spontaneously and eventfully on April 6, 1950. Sixteen hours after delivery, a bilateral tubal ligation, using Pomeroy's operation, was done with the patient under continuous peridural anesthesia. At operation it was noted that the veins of the broad ligament were extremely large, and double ties were used about each loop of resected tube. The patient had an uneventful postoperative course and was discharged on the eighth postpartum day. The next day she returned with a rather sudden onset of right lower subscapular pain that radiated through her chest. A roentgenogram that was taken was read at the time as being negative, but subsequently on review of the film there was found a triangular shadow in the right costophrenic angle. The patient was sent home and was readmitted to a county hospital for three days, but again no significant objective findings were noted, although the patient continued to complain of chest pain. On April 20, 1950, the patient died suddenly, the terminal episode being

marked by a sudden onset of excruciating retrosternal pain and severe cyanosis. No autopsy was obtained. The final clinical impression was death due to pulmonary embolism, previous pulmonary infarction, pelvic phlebothrombosis, postoperative tubal ligation, and bilateral and great multiparity.

A 29-year-old nonwhite woman was referred from a county clinic for delivery and sterilization. The indication for tubal ligation was great multiparity. On Feb. 8, 1947, she went into labor and after two hours and 53 minutes, spontaneously delivered a 6 lb. 1 oz. (2,750 gm.) infant. Within 24 hours after delivery, bilateral Pomeroy's operation was performed under thiopental sodium anesthetic. The postoperative course was normal, and the patient was discharged on the seventh day after surgery. In October, 1954, the patient was submitted to autopsy by the medical examiner. The cause of death was right tubal ectopic pregnancy.

Observations.—In evaluating the start of ambulation it is difficult to make an accurate statement because of the large number of patients with complicated operations plus varying views of different surgeons relative to the merits of early ambulation. However this may be, 36.87% of the patients were ambulatory by the second postoperative day and 59.94% by the fifth day. Significant is the finding that in 86.79% there was no delay in ambulation because of the operation; intercurrent disease delayed ambulation in 4.89%; postpartum and/or postoperative complications delayed ambulation in only 8.2% of the patients. The majority of the patients were discharged 6 to 10 days after surgery and 7 to 11 days after childbirth. Some interesting findings were revealed in studying the effect of surgery on breast-feeding. Breast-feeding was carried out by 56.16% of the patients; only in 7.24% was breast-feeding a failure, and this may possibly be attributed to surgery. Of the segments of fallopian tube received in the laboratory 770 (75.36%) were normal, and in 86 cases salpingitis was present.

TABLE 3.—*Types of Operation*

	Cases	
	No.	%
Pomeroy		
Puerperal sterilization	1,022	
At cesarean section or hysterotomy	400	80.77
6 or more weeks post partum or never pregnant	56	
Irving	206	11.25
Madlener	41	2.24
Cornual excision	27	1.48
Atypical operation	18	0.98
Salpingectomy	5	0.27
Other	55	3.01
Total	1,830	100.00

TABLE 4.—*Time from Delivery to Puerperal Sterilization by Pomeroy Technique*

Time, Hr.		Cases No.	Cases %	
1- 6	(1st day)	156	15.26	52.72
7- 12	(1st day)	148	14.48	52.72
13- 18	(1st day)	109	10.66	52.72
19- 24	(1st day)	126	12.32	52.72
25- 48	(2nd day)	244	23.88	
49- 72	(3rd day)	99	9.67	
73- 96	(4th day)	43	4.20	
97-120	(5th day)	30	2.93	
121-144	(6th day)	17	1.66	
145-168	(7th day)	10	0.97	
Beyond 169	(8th day or beyond)	38	3.71	
Unknown		2	0.19	
	Total	1,022	99.93	

LONG TERM FOLLOW-UP

In attempting to study the 1,830 patients who were sterilized, a questionnaire was sent to each one. A follow-up of 1,022 (55%) was obtained. In this group 939 patients had no subsequent difficulty, 47 had abnormal menses, 10 had psychotic manifestations, and 3 patients had both psychotic and menstrual difficulty; 74 patients had subsequent pelvic surgery done elsewhere, an incidence of subsequent laparotomy of 9.29%; 1,005 patients had no pregnancy after sterilization; and during this follow-up period, which varied from 4 to 14 years, there were 17 failures, 1.7% of the cases observed, in 4 of these the pregnancy was tubal.

TABLE 5.—*Sterilization Failures**

Case	Operation	Indication	Operator	Date	Interval Between Sterilization and Subsequent Pregnancy, Mo.
	Pomeroy Sterilization Failures—Puerperal (Failure Incidence, 1:340)				
1	Postpartum Pomeroy sterilization	Multiparity	Intern	May, 1949	36.5
2	Postpartum Pomeroy sterilization	Multiparity	Assistant resident	July, 1950	35 †
3	Postpartum Pomeroy sterilization	Multiparity	Intern	Feb., 1947	90 †
	Pomeroy Sterilization Failures—Accompanying Cesarean Section or Hysterotomy (Failure Incidence, 1:57)				
4	Hysterotomy Pomeroy sterilization	Rheumatic heart disease	Resident	Jan., 1946	6
5	Hysterotomy Pomeroy sterilization	Preeclampsia, severe	Full-time staff	April, 1946	14
6	Cesarean section Pomeroy sterilization	Placenta previa High parity	Resident	Sept., 1946	46.25
7	Cesarean section Pomeroy sterilization	Repeat section Contracted pelvis	Assistant resident	Nov., 1945	12
8	Cesarean section Pomeroy sterilization	Previous section Poor obstetric history	Assistant resident	Oct., 1946	4.5
9	Cesarean section Pomeroy sterilization	Previous section Breech	Assistant resident	Aug., 1949	29
10	Cesarean section Pomeroy sterilization	Third section	Assistant resident	March, 1949	52.5
	Sterilization Failures—Other Techniques				
11	Cesarean section "Silk" sterilization technique	Previous section Contracted pelvis	Resident	Aug., 1947	34 †
12	Cesarean section Madlener sterilization	Rheumatic heart disease	Resident	Sept., 1936	19
13	Hysterotomy Madlener sterilization	Chronic nephritis	Assistant resident	June, 1936	13
14	Hysterotomy Madlener sterilization	Heart disease	Visiting staff	April, 1938	38 †

* Three additional failures occurred; only one tube ligated.
† Culminated in an ectopic pregnancy.

Failures.—Table 5 shows the high incidence of sterilization failure when the Pomeroy operation was done at the time of cesarean section or hysterotomy (1:57) as compared with a much lower rate (1:340) in the "puer-

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peral sterilization" group. We are at a loss to explain this difference, but consider it most important, for it is in the former group, and particularly in patients in whom hysterotomies have been performed that one sees the acutely ill patient in whom future childbearing is strongly contraindicated. Although we have no explanation for this surprising difference, we have been sufficiently impressed by it to abandon the Pomeroy procedure at cesarean section and hysterotomy in favor of the Irving technique. Moreover, in view of the two ectopic pregnancies that occurred after the Pomeroy operation, one of which was fatal, it is our opinion that the Irving technique is probably preferable in all cases unless haste is mandatory. Another noteworthy finding in respect to the failures, and equally surprising, is the long interval between some sterilizations and subsequent pregnancies, i. e., from 4.5 to 90 months. This is also without known reason. One must deduce from this finding that, when judging the merits of a particular sterilization procedure, many years must elapse before an accurate evaluation can be made.

From a practical viewpoint perhaps the most important finding in this series of failures is the high incidence of ectopic pregnancies, with one death due to this cause. Almost one-fourth of the failures took the form of tubal gestations. Moreover, since the interval between operation and the development of ectopic pregnancy may be as long as seven and a half years, it is possible that some of the sterilizations performed in the terminal years of the study may yet culminate in this complication. When it is also recalled that two additional women died from pulmonary embolism, giving a total death rate in 1,022 puerperal Pomeroy ligations of 1 in 340, it is clear that this operation is by no means an innocuous procedure but is associated with definite hazards both immediate and remote. To justify on medical grounds any sterilizing operation simply because of great multiparity, it must be established beyond question that the risk of death from continued fertility is decidedly greater than the risk of death from the sterilizing operation. When, in 1936, we first adopted the policy of sterilizing mothers with a parity of eight or more, the maternal death rate in these grande multiparas was doubtless several times that reported in this paper for the Pomeroy operation. Today, however, with improved obstetric care, especially more efficacious methods of combating blood loss (a frequent cause of death in this group), it seems dubious whether the frequency of death from childbearing in these women of high parity is appreciably higher, if it is higher at all, than the one death in 340 patients reported in this paper for puerperal Pomeroy sterilization.

It is barely possible, of course, that some other technique of sterilization, or indeed the Pomeroy operation itself in more experienced hands, would yield better results in respect to failures, ectopic pregnancies, and deaths. As far as we are aware, however, this possibility has not been documented by any large series with a 5 to 10 year follow-up. Until such proof of the superiority of other techniques is available, it is our carefully weighed opinion, on the basis of the evidence submitted, that great multiparity alone does not constitute a true medical indication for sterilization.

SUMMARY AND CONCLUSIONS

At the department of obstetrics of the Johns Hopkins Hospital 1,830 puerperal tubal ligations were performed between 1936 and 1950. The chief indications were great multiparity, chronic hypertension, and repeated cesarean section, "great multiparity" being defined as "eight or more previous viable deliveries." The average number of deliveries that had been experienced per patient at the time of the operation was 6.7 and among the "great multiparity" group, 10. In 1,478 cases (80.8%) the Pomeroy technique was used. Of these Pomeroy operations 456 were done at either cesarean section or hysterotomy or six weeks or more after delivery. In the remaining group of 1,022 cases (designated here as the puerperal sterilizations) the procedure was carried out early in the puerperium, 76.6% having been performed within the first 48 hours. There were a total of 166 operators, mostly house staff members. A questionnaire follow-up of all 1,830 cases was carried out 4 to 14 years after the operation. There were a total of 17 failures to prevent pregnancy, a ratio of 1:108 operations. A more detailed analysis of these failures brought to light three very striking and surprising findings. 1. In the 1,022 early puerperal sterilizations by the Pomeroy technique there were three failures, a ratio of 1:340 operations, whereas in 400 cases in which the Pomeroy procedure accompanied cesarean section or hysterotomy, there were seven failures, a ratio of 1:57 operations. We have no explanation for this pronounced difference, but on these grounds have abandoned Pomeroy sterilization at cesarean section or hysterotomy, and are using the Irving technique instead. 2. Another striking finding was the extreme length of the period that sometimes intervenes between tubal sterilization and pregnancy, this interval being 90 months in one of our cases and over 56 months in two others. 3. Four of the failures culminated in ectopic pregnancies, two after puerperal Pomeroy ligation, one after a Madlener operation, and one after an atypical silk technique. One of these ectopic pregnancies terminated fatally.

In addition to the death from ectopic pregnancy, two women died from pulmonary embolism, a death rate of 0.3% in 1,022 puerperal Pomeroy sterilizations. The Pomeroy operation, therefore, is not an innocuous procedure but carries definite risks both immediate and remote. The conclusion is reached that these hazards approximate those imposed by undisturbed fertility and that sterilization because of great multiparity alone cannot be justified on medical grounds.

The Patient Must Not Be Neglected.—A physician is free to choose whom he will serve. He should, however, respond to any request for his assistance in an emergency or whenever temperate public opinion expects the service. Once having undertaken a case, the physician should not neglect the patient, nor should he withdraw from the case without giving notice to the patient, his relatives or his responsible friends sufficiently long in advance of his withdrawal to allow them to secure another medical attendant.—Principles of Medical Ethics of the American Medical Association, chapter 2, section 4, June, 1954.

SYPHILIS IN INDUSTRY

John Godwin Downing, M.D., Boston

Although syphilis is an old disease, it took industrialists a long time to realize their responsibility regarding it. Serious accidents and financial losses finally prompted action. In 1920, the Association of Railway Surgeons adopted a resolution for cooperation with the Public Health Service in syphilis control. This action was prompted in two ways. In the first place, the increased speed of trains demanded good health in those responsible for safety. Secondly, the workers were alarmed because payment of beneficiaries suffering from late syphilis was rapidly depleting the treasury of their brotherhood. Later, the increasing publicity about syphilis aroused the public and caused unwarranted alarm, with resulting demands for increased precautions regarding those in charge of transportation and those having personal contact with the public, such as food handlers, barbers, hairdressers, and the like. As a result considerable agitation arose concerning the employability of these individuals, and considerable injustice occurred regarding their status.

Industry became a first line of attack in the organized campaign against syphilis. As might be expected, the greatest incidence of acute syphilis was found among young workers. In the older group occurred the late cases, with a fairly high incidence of cardiovascular syphilis among those doing heavy work and with neurosyphilis frequent among those doing clerical or executive jobs. Both forms of the disease have been expensive for employers. Industrial accident board hearings became frequent for claims following trauma, which revealed the underlying syphilitic ulcers, fractures, gummata of bones, eye lesions, cerebrospinal manifestations, and aneurysms. The recent national campaign for control of syphilis inundated readers with innumerable reports in both lay and medical journals. The campaign was a success, at least on the surface.

When the committee preparing a symposium on syphilis to be reported at the American Academy of Dermatology and Syphilology requested me to obtain some data on the present problem of syphilis in industry, I accepted this assignment with interest, because I was curious to know how syphilis as an industrial problem was affected by penicillin and other antibiotics. For the past five years or so it has been reported that syphilis is no longer a problem. Syphilologists were seeing fewer patients, and referrals from local practitioners were drastically reduced. Attendance at public clinics was sharply diminished, and in some parts of the country the public health officials closed them. In some areas venereal disease control activities were shared or combined with other functions of public health departments. An attitude of complacency had set in. On the other hand, many physicians warned of the dangers of premature rejoicing; while the incidence of syphilis was being reduced, the battle was by no means over. It is estimated that at the present time there is a reservoir of over 2 million people in this country who need treatment for syphilis. During the year 1953, about 91,000 civilians acquired syphilis, of whom some 10% were reported and treated for primary and secondary syphilis. It is no wonder then that responsible public health officials and physicians have repeatedly warned us to adopt a realistic stand on syphilis. They prophesied a resurgence of this disease if efforts were relaxed too soon. It is interesting to note that in 1953, 18 states and the District of Columbia reported an increase in infectious syphilis.[1]

PREVALENCE OF SYPHILIS

A search of the literature revealed a dearth of recent information on the subject of syphilis in industry. I then wrote to a large number of medical directors of various industrial plants asking them for this information. Most of these directors felt that syphilis was not a problem, while others said it was worthwhile screening their employees even for the few cases that might be uncovered. Interestingly enough, this sense of security was fostered by the fact that the incidence of positive reactions in these industries was only 1%, or about one-half of what it had been 10 years ago. The prevalence of syphilis in industry has always been difficult to estimate. About 10 years ago it was estimated at 2 million cases. Assuming that 30% of the adult population is employed in all kinds of industry, and that the prevalence rate among workers is the same as that in the general population, there would be 600,000 industrial workers with syphilis. Such a crude estimate is subject to considerable error, particularly in assuming prevalence to be proportional to population. No attempt has been made to determine whether any difference does exist between the prevalence rate for industrial workers and persons not in industry. Available data are not clear on this point, the main difficulty being that occupational rather than industrial groupings were used for study.[2] In 1943, Howles [3] cited estimates that exclusive of women workers, syphilis was responsible for the loss of 21 million work days each year, amounting to 84 million dollars. Compensation payments have been made for alleged industrial disabilities, although occasionally a syphilitic disease and not the occupation was responsible.

One organization, which employed more than 36,800 persons in various plants in 17 states, established a central serologic laboratory, and all new employees were required to submit to a test. Older employees were permitted to submit or not as they wished, but less than 10% refused. In all employees examined, 1,488, or 4%, had positive tests. As a result of venereal disease control instituted through funds from the federal government many plants instituted preemployment serologic tests and routine tests during periodic or annual physical examinations of the employee, regardless of socioeco-

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Read at the meeting of the American Academy of Dermatology and Syphilology, Chicago, Dec. 8, 1954.

1. Today's VD Control Problem: A Joint Statement to the Appropriations Committee of the Federal Congress, 1954, Am. J. Syph. 38: 161-175 (May) 1954.
2. Dutchess, C. E.: Personal communication to the author.
3. Howles, J. K.: A Synopsis of Clinical Syphilis, St. Louis, C. V. Mosby Company, 1943 p. 486.

nomic status. One life insurance company instituted tests among 13,000 home office employees at their annual physical examination, continuing them for two years. The number of employees who had doubtful or positive reactions in one or both years amounted to 304, an average of 1.42% per year. Many of these cases were considered to have a nonspecific serology.[4] It is interesting to note that in my private practice, among industrial workers referred for questionable occupational disease of one type or other, routine serologic tests revealed 1.5% positive reactions.

A comparison of statistics is also interesting. In 1920, C. Morton Smith,[5] the noted syphilologist, published a paper in which he lamented the fact that active syphilitic lesions were so rare that it was impossible to find sufficient clinical material for teaching students. He attributed this rarity to four factors: early diagnosis, better treatment, prohibition, and education. His figures were apparently based on the syphilis rate of 1919, during which year 100,466 cases were reported, or 96.3 per 100,000 population. During this time prohibition was actually in effect, and it was practically impossible to secure intoxicating beverages without a federal permit. There was no such thing as a bootlegger. However, the situation was rapidly taken care of, and the illegal flow of whiskey was instituted and speedily increased. Coincidentally, the rates of syphilis soared from a low of 100,466 cases in 1919 to a high of 238,656 in 1933 when prohibition was repealed, an increase of 137%.[6] However, there were other factors to account for this increase. After the repeal of prohibition in 1933, the reported incidence of syphilis in the civilian population continued to climb, reaching a peak of 575,593 cases in 1943.[1] Over these years there was a decline in the moral caliber of the country, manifesting itself by many signs, one of which was an increasing degree of sexual promiscuity. The sexual mores of the people sank to a low ebb. Nationally, the illegitimate child rate was about 4% of total live births. In Massachusetts my colleagues and I reported on the first 1,005 deliveries that were part of our prenatal syphilis study at the Boston City Hospital; 4% of the mothers admitted that they were single, and, undoubtedly, many more of the series were illegitimately pregnant.[7] In the field of juvenile delinquency, the third most common cause of arrest in 1952 was "sexual activities." Why has prostitution decreased in the United States? Law enforcement and the pressure of public opinion are partial answers. More important is the competition from the increasing number of the noncommercialized promiscuous amateurs. The prostitute is no longer a major factor in the venereal disease control problem. She has been replaced by the amateur. With the advent of penicillin and its short-term treatment, whatever fear the amateur had of long and arduous treatment lasting for a year and a half, was completely dissipated. Whatever effect the arsenical and bismuth era had in preventing sexual promiscuity no longer exists. Promiscuity in this country is on the increase. Penicillin will not eradicate syphilis, for no disease in the history of man has been treated out of existence.

Whatever reduction in the syphilis rate in this country has been achieved has been due to two factors. The first of these is the organization and efficient functioning of venereal disease control activities throughout the United States. Here we see the effects of the funds expended by federal, state, and local governments in finding the contacts of persons with active syphilis and bringing them to treatment. Second is the effect of penicillin in rapidly reducing the infectiousness of syphilis and providing an early and adequate cure. However, in spite of these funds and wonder drugs, the reported syphilis rate in the United States in 1953 was 100.8 per 100,000, whereas in 1919, without organization and without funds, the rate was 96.3 per 100,000.[1] Recently the federal government drastically cut its budget and reduced the grants-in-aid for venereal disease control to the states and local communities. This was short-sighted economy. Many states and communities no longer provide epidemiological services in tracing contacts of persons with active syphilis. The authorities have lost sight of the fact that there is an infectious reservoir of venereal disease still remaining in our communities. The sexual mores of our people, being what they are, will further increase this reservoir. If control efforts are relaxed through overoptimism and penny-pinching and if the present level of sexual promiscuity persists, one can predict epidemics of these diseases in the future.

The curtailment of federal grants to the states was reflected in industry. Many state health departments that had previously performed serologic tests for syphilis without charge for industrial physicians ceased doing so; for example, New York state. Industrial medical departments were unwilling to use their meager budget to have these tests done by private laboratories. As a result, many industries stopped performing these tests. In plants with full-time medical directors, where preemployment and periodic examinations were performed, a routine test of blood, urinalysis, vision testing, hemoglobin determination, and other simple tests were part of a screening of the employee. Many of these examinations are the result of previous routine performance of more limited tests such as the serology test for syphilis or roentgenographic examination for tuberculosis. Certification by the American Academy of Occupational Health postulates the routine serology. Some plants still maintain this preemployment serology, for they are convinced that in the long run it is worthwhile. Several medical directors have stated that they believe the restricted budgetary measures are short-sighted, and despite the dramatic advance in therapy, the incidence of syphilis is increasing in the industrial population.

A consideration of a few statistics is revealing. In an industry where the socioeconomic status of the employee is on a high plane, there is an apparent improvement in the over-all picture. For example, from one plant come

4. Abstract of the Proceedings of the Fifty-First Annual Meeting of the Association of Life Insurance Medical Directors of America, vol. 27, New York, Press of Recording and Statistical Corporation, 1941, p. 30.

5. Smith, C. M.: The Vanishing Lesion: A New Problem in Teaching, Arch. Dermat. & Syph. **2**: 639-648 (Nov.) 1920.

6. VD Fact Sheet, Issue 10, U. S. Department Health, Education, and Welfare, Public Health Service, Dec., 1953, p. 13.

7. Fiumara, N. J.; Fleming, W. L.; Downing, J. G., and Good, F. L.: The Incidence of Prenatal Syphilis at the Boston City Hospital, New England J. Med. **247**: 48-52 (July 10) 1952.

the figures shown in table 1.[8] The state of Connecticut shows an interesting tabulation of the number of serologies taken during the past five years (table 2). On the other hand, a high syphilis rate is found among low socioeconomic groups. In Connecticut, where the law requires compulsory examination of persons accused of

TABLE 1.—*Results of Mass Blood Testing for Syphilis in Industry A* *

Year	No. Taken	Positive		Doubtful	
		No.	%	No.	%
1949	1,543	2	0.13	..	....
1950	2,216	5	0.23	2	0.09
1951	4,998	18	0.36	4	0.08
1952	1,469	..	....	..	....
1953	1,082	1	0.09	..	....
Total	11,308	26	0.23	6	0.05

* Source requested that industry not be identified.

vice charges, out of a total of 7,083 examinations from 1944 to 1952, 897, or 12.6%, revealed infection with venereal disease—9.3% syphilis and 3.3% gonorrhea. For the fiscal year 1952, 10% of those examined had syphilis.[9] In New Jersey, where Shepard blood-tested 3,170 agricultural migratory laborers, 414 (13.1%) had positive reactions and 385 (12.1%) had doubtful reactions, or a total of 25.2% with positive or doubtful tests.[10] Fiumara in Massachusetts, examining 91 agricultural migratory workers in Middlesex County, found that 3.3% had syphilis. However, the figures in two plants are interesting, showing a low incidence up to 1953, but from January to July, 1954, a definite increase in positive reactors is noted[11] (tables 3 and 4). In certain areas, however, the percentage of positive reactors did not fall as low as in other areas[12] (table 5).

TABLE 2.—*Serologic Specimens Taken by the Bureau of Industrial Hygiene, Connecticut State Health Department, 1949-1953*

		No. of Specimens	Reactive Specimens	
			No.	%
1949	All types	306,120	12,333	4.0
	Industrial	35,708	522	1.5
1950	All types	364,658	10,856	3.0
	Industrial	56,326	595	1.1
1951	All types	418,256	10,974	2.6
	Industrial	76,836	949	1.2
1952	All types	400,729	12,681	3.2
	Industrial	70,252	1,268	1.8
1953	All types	398,288	11,683	2.9
	Industrial	70,004	804	1.1
Grand total	All types	1,888,051	58,527	3.1
	Industrial	309,126	4,138	1.3

Selected case findings in syphilis control show the value of continued screening techniques (table 6). The Cumberland County Health Department screened 9,093 persons out of a population of 65,000 (aged 15 to 70) and found 738 reactors. In other words, by careful screening of 14% of the population, 39% of the estimated total reactors in the county were found. Unskilled worker groups contributed the most reactors and skilled laborers and professional workers the fewest.[13]

VALUE OF EDUCATION IN SYPHILIS CONTROL

In 1920 C. Morton Smith[5] mentioned the value of education in the control of syphilis. Education for the average person has enabled the workers in this field to publicize facts, with remarkable improvement in the control of this disease; however, apparently this education has not penetrated to employers and certain medical directors. It would seem that in this enlightened day employers would depend on their medical directors for the evaluation of whether a person with a positive serology is a useful worker. All syphilologists doing industrial

TABLE 3.—*Results of Mass Blood Testing for Syphilis in Industry B* *

Year	Total	No. of Tests					
		Positive		Doubtful		Positive and Doubtful	
		No.	%	No.	%	No.	%
1949	4,044	91	2.25	17	0.42	108	2.67
1950	4,843	102	2.10	9	0.19	111	2.29
1951	4,734	57	1.20	18	0.38	75	1.58
1952	4,890	48	0.98	36	0.74	84	1.72
1953	4,717	31	0.66	32	0.68	63	1.34
Total	23,234	329	1.42	112	0.48	441	1.90
Jan. to July, 1954	2,037	19	0.93	20	0.98	39	1.91

* Source requested that industry not be identified.

work have always found a positive serology embarrassing. The earlier literature was filled with cases of injustice. At that time employers went by the findings of such a reaction. Reporting to the insurer always convinced him that the eruption, no matter what it was, must be syphilis. This often started a rumor that reached the employer, with subsequent discharge, despite the dermatologist's protestations of noninfection. It also handicapped the worker in finding new employment. While recent education has been valuable both to the employer and the employee, the situation still remains embarrassing. This was evidenced by the situation that developed recently in Cincinnati, a city that was previously cited as a shining example of syphilis control.

According to a letter received by the chairman of the Academy of Medicine of Cincinnati, a large number of industries in the city had an employment policy that barred from work any individual who had a positive serology, on the fallacious assumption that this indicated acute syphilis. The writer[14] stated that while over and over again a man or woman with syphilis, either acquired or congenital, and properly treated, was permitted by state law and modern medical practice to marry, he or she was refused employment because the qualitative Wassermann, Kahn, or Kline test was reported positive. He took up this matter with personnel managers and was told that this archaic policy was formulated by the advisors of the company. These officials, he said, asked

8. Thompson, R. C.: Personal communication to the author.

9. Talbot, H. P.: Vice Examination and Control of Syphilis, Connecticut Health Bull. **67**: 198-199 (July) 1953.

10. Shepard A. C., and Page, W. J., Jr.: Venereal Disease in Agricultural Migrants: New Jersey, 1953, Pub. Health Rep. **69**: 831-835 (Sept.) 1954.

11. McGovern, E. A.: Personal communication to the author. Mangelsdorf, A. M.: Personal communication to the author.

12. Gallivan, J. N.: Personal communication to the author.

13. Moore, G. and Foster, M. T.: Selective Case Finding in Syphilis Control, Pub. Health Rep. **68**: 167-172 (Feb.) 1953.

14. King, A. G.: Personal communication to the author.

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how it was known that antibiotics really cured syphilis and declared that other persons would refuse to have personal contact with a man known to have syphilis, and that they could not take chances with such a man. The writer declared that this unenlightened employment policy made the medical profession look ridiculous. He requested that steps be taken to enlighten such employers.

The council of the Academy of Medicine of Cincinnati submitted this letter to a group of competent syphilologists and to the Cincinnati Dermatological Society for their comments. Suitable recommendations were made and were approved by the Committee on Industrial Medicine and Health and the Medical Committee of the Procter and Gamble Company. It was proposed that the matter be brought to the attention of the medical profession of Cincinnati and to industrial medical departments and the Cincinnati Public Health Department. The comments and recommendations were carefully worded and included the recent facts regarding the present-day knowledge of the serologic test for syphilis and the various clinical stages of this disease. The Committee agreed that nobody should be refused employment solely because

TABLE 4.—*Results of Mass Blood Testing for Syphilis in Industry C* *

Year	Total Serologies	Negative Serologies		Positive Serologies	
		No.	%	No.	%
1950-1952	740	715	96.62	25	3.38
1953	1,748	1,738	99.43	10	0.57
1954 (6 mo.)	450	433	96.22	17	3.78
Grand total †	2,938	2,886	98.23	52	1.77

* Source requested that industry not be identified.
† January, 1950, to June, 1954.

of a positive serologic test for syphilis. The interpretation of the serologic status of an individual can be made only by a physician and may occasionally be a complex problem requiring the services of an expert. Under no circumstances should the employability of an individual with a positive serologic test for syphilis be made by lay persons who pass on the other qualifications of the prospective employee, and there is even the question of violation of the privileged communication statute under such conditions. The certificate of a physician that the sero-positive individual is noninfectious and physically employable should suffice.[15]

This is no new problem. Many years ago Joseph Earl Moore,[16] head of the Syphilis Clinic of Johns Hopkins Medical School, stated, "So far as is known, there is, except in rare instances, no good evidence to indicate that a syphilitic worker is any more likely, (a) to be involved in accidents than his non-syphilitic brother; or (b) if involved in an accident, to suffer any more serious or prolonged disability; or (c) to suffer more severely from intercurrent non-syphilitic disease; or even (d) to undergo material shortening of his life span. Whatever risk there may be against any of these eventualities may be largely guarded against except in cardiovascular or neurosyphilis by adequate treatment."

It is too early to know whether the complications of specific cardiovascular and cerebrospinal disease can be entirely prevented by the use of the newer combinations of treatment, but the present results indicate that they can largely be controlled. In certain industries, such as the railroads and commercial air lines, preemployment blood tests have been advocated for train men and pilots, partly on the basis of possibly preventing serious accidents from man failure due to active cerebrospinal disease. Such a possibility seems remote, as these employees

TABLE 5.—*Results of Mass Blood Testing for Syphilis in Industry D* *

Year	Total			Male			Female		
	No. Tested	Positive		No. Tested	Positive		No. Tested	Positive	
		No.	%		No.	%		No.	%
1949	6,222	29	0.47	5,508	25	0.45	714	4	0.56
1950	11,177	34	0.30	8,630	27	0.31	2,547	7	0.27
1951	22,639	87	0.38	16,929	81	0.48	5,710	6	0.11
1952	14,738	72	0.49	12,455	68	0.55	2,283	4	0.18
1953	19,830	102	0.51	15,373	89	0.58	4,457	13	0.29
1954 †	6,065	22	0.36	5,070	20	0.39	995	2	0.20

* Source requested that industry not be identified.
† Taken from January to April.

are examined at least annually, and any indication of such a development should be picked up in the 10 to 20 years elapsing between the time of primary infection and the late complication.

The writer of a recent résumé states that in using the 1953 figures as a basis for evaluation, i. e., one new case of recent or old infection reported per 1,000 of population, he thinks we may agree that the percentage does not suggest a valid reason for doing routine preemployment serologic tests.[17] It must be recognized, however, that there are sufficient exceptions to the above figures, particularly in certain socioeconomic and geographical groups, to indicate such routine testing as a screening procedure in lieu of history taking and physical examination, or when the suspected or known incidence of disease is higher than average, and the facilities for running the tests are readily available and comparatively inexpensive.

TABLE 6.—*Percentage of Syphilis in Mass Blood Testing at Selected Industries in Atlanta, Ga.*

Industry	1950					
	White Positive and Doubtful			Negro Positive and Doubtful		
	Total	Male	Female	Total	Male	Female
Manufacturing	2.3	2.3	2.1	26.0	25.4	28.1
Utilities	1.2	1.4	1.0	21.4	23.9	10.2
Government	1.5	1.8	1.0	18.7	18.2	25.0
Offices and stores	1.0	0.8	1.1	21.5	22.4	19.7
Total tested	1.9	2.2	1.6	19.9	19.6	20.1

SUMMARY

With a reservoir of about 2 million persons in the community needing treatment, and with 156,099 patients reported in 1953, and considering the sexual mores of our people, syphilis will remain with us for some time to come. In industries employing highly skilled workers, members of the higher socioeconomic groups, the discovery rate for syphilis will be admittedly small. However, the cost of finding even these few is worth while to

15. Weiner, A. L.: Positive Blood Tests for Syphilis and Employability, editorial, Cincinnati J. Med. **34**: 245-246 (July) 1953.
16. Moore, J. E.: Syphilis and Unemployment, editorial, Am. J. Syph. **21**: 339-343 (May) 1937.
17. Graham, R. M.: Personal communication to the author.

the industry, because it will not only retain the services of a highly trained individual, but also eliminate unjustifiable claims for disabilities that are not due to occupation but rather to syphilis. For industries employing less skilled laborers or laborers of the low socioeconomic groups, or industries located in high syphilis prevalence areas, the blood test becomes even more important as a part of the routine preemployment examination. There is need even today to educate management regarding the employability of syphilitics or persons found to have a positive serologic test for syphilis who have no medical defect that would prohibit them from carrying out assigned duties. The advisability of employing such employees should not rest on lay authority, but should be decided by competent physicians. The new antibiotics have done a tremendous job in speeding up the cure of syphilis, but there is much more to be done. Any attempt to reduce or abandon the control efforts by public health authorities is not only shortsighted but foolhardy.

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CLINICAL NOTES

IMMUNIZATION ADENITIS

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The regional adenitis following vaccination with smallpox virus or with BCG is well known to the medical profession. Less well known is the regional adenitis following immunization with other antigens, such as pertussis vaccine, diphtheria toxoid, and tetanus toxoid. Glands in the axilla or groin, depending upon the site of injection, are almost invariably enlarged to the point of being easily palpable. However, we could find no report in the literature of large regional glands following such immunization. For this reason, two cases of marked axillary adenitis, due in all probability to the injection of antigens for immunization, are reported.

REPORT OF CASES

CASE 1.—The patient was injected with whooping cough vaccine at 5, 6, and 7 months of age, and at 8 months of age combined diphtheria-tetanus toxoid injections were given at monthly intervals. Three days after the first toxoid injection a mass approximately 2.0 by 2.5 cm. could be felt in the left axilla, slightly tender and freely movable. This disappeared in two weeks. The second injection of combined toxoids was given, by error, in the same arm, and again two days later a left axillary mass became palpable, 4 by 4 cm., slightly tender but freely movable. The mass persisted for two months. To exclude the possibility of a lymphoma, a biopsy was done, which was interpreted as showing a simple hyperplastic adenitis. After one month more, the mass could no longer be palpated.

CASE 2.—The patient was injected at 6, 7, and 8 months of age with the usual triple immunization mixture of antigens, first in the right arm, then in the left, and then again in the right. Four days after the third injection, a mass in the right axilla was discovered, about 3.5 by 2.5 cm., freely movable, and not tender. Since resolution of the mass was slow, after four weeks a biopsy was done, and review of the slide by the National Tumor Board resulted in a diagnosis of immunization adenitis.

In neither case was there any fever or other signs of a generalized reaction, nor was there any marked redness or tenderness over the swellings. The biopsies were done long after the possibility of recovering viable organisms was past. The symptoms and signs, however, were not as severe as those commonly encountered in a pyogenic infection of the glands.

While it is well known that the regional lymph nodes are probably the first affected by the antigens used for subcutaneous inoculation, there is little discussion in the pediatric literature. Ehrich and his co-workers,[1] using fractions of Hemophilus pertussis vaccine in lethal doses in 15 rabbits, found only 2 whose glands showed extensive necrosis with diffuse hemorrhages throughout the parenchyma, but in most animals the nodes were markedly hyperemic and the central sinuses were sometimes distended with lymph. The role of the regional glands after immunization with pneumococcic and streptococcic vaccines was reported by deGara and Angevine [2] and with other antigens by Harris and Harris,[3] Hellman and White,[4] and Østerlund.[5] Ringertz and Adamson,[6] using vaccines of beta-hemolytic streptococci as well as of Micrococcus (Staphylococcus) pyogenes var. aureus, reported histological studies of intense hyperplasia and activity in the regional lymph nodes.

Probably the best discussion of the whole subject is that of Ehrich [7] in a report of the A. M. A. Council on Pharmacy and Chemistry on tissue reactions from antigens. He makes the point that the introduction of an antigen into tissue causes an inflammatory reaction and that this may lead to hemorrhage, necrosis, suppuration, or other undesirable changes locally or in the regional lymph node. These begin to appear on the third or fourth day and reach their highest concentration on the sixth or seventh day. The production of axillary or inguinal glands large enough to produce concern sufficient to warrant a biopsy is undoubtedly rare; however, it seems reasonable to change the site of injection each time to avoid this possibility.

SUMMARY

In two infants enlarged axillary glands appeared within a few days after immunization with whooping cough vaccine, diphtheria, and tetanus toxoids. Biopsy in both cases was interpreted as showing a hyperplastic response to the immunization antigens.

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1. Ehrich, W. E.; Bondi, A., Jr.; Mudd, S., and Flosdorf, E. W.: The Tolerance of Rabbits for the Agglutinogen and the Toxins of Hemophilus Pertussis, Am. J. M. Sc. **204**: 530, 1942.

2. deGara, P. F., and Angevine, D. M.: Studies on the Site of Antibody Formation in Rabbits Following Intracutaneous Injections of Pneumococcus or of Streptococcus Vaccine, J. Exper. Med. **78**: 27, 1943.

3. Harris, T. N., and Harris, S.: Histochemical Changes in Lymphocytes During the Production of Antibodies in Lymph Nodes of Rabbits, J. Exper. Med. **90**: 169, 1949.

4. Hellman, T., and White, G.: Das Verhalten des Lymphatischen Gewebes während eines Immunisierungsprozesses, Virchows Arch. f. path. Anat. **278**: 221, 1930.

5. Østerlund, G.: Die Reaktion des lymphatischen Gewebes Während der Ausbildung Immunitat gegen Diphtheria toxin—Thesis, Acta path. et microbiol. scandinav., supp. 34, 1938.

6. Ringertz, N., and Adamson, C. A.: The Lymphadenitis Picture in Man with Various Types of Bacterial Invasion, Acta path. et microbiol. scandinav. **25**: 192, 1948. Ringertz, N., and Adamson, C. A.: The Lymph Node Response to Various Antigens, Acta path. et microbiol. scandinav., supp. 86, p. 1, 1950.

7. Ehrich, W. E.: Significance of the Tissue Reactions Caused by Antigens, report of the Council on Pharmacy and Chemistry, J. A. M. A. **135**: 94 (Sept. 13) 1947.

PREDNISONE IN TREATMENT OF SELECTED DERMATOSES

PRELIMINARY REPORT

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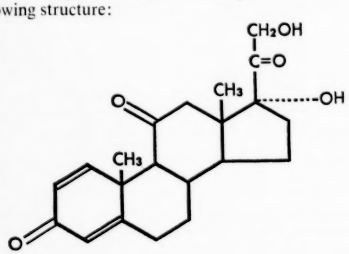
Bunim and his co-workers recently reported [1] the value of two new synthetic steroids, prednisolone and prednisone, formerly known as metacortandralone and metacortandracin, in the treatment of rheumatoid arthritis. Their preliminary studies indicated that these synthetic steroids possess both antirheumatic and anti-inflammatory action and apparently resemble an adrenal cortical hormone in that they both produce a prompt, significant fall in number of circulating eosinophils and a suppression of urinary 17-ketosteroids. These investigators concluded that these new steroids have three to four times the potency of cortisone without producing any increase in severity or frequency of side-effects. They noted no apparent change in electrolyte balance. In their series, patients who failed to respond to cortisone, hydrocortisone, or corticotropin (ACTH) showed marked improvement with relatively small doses of the new synthetic compound. Prednisone is a synthetic chemical compound that has the following structure:



It is produced by dehydrogenation of the cortisone nucleus at positions 1 and 2. It is a white, crystalline, amorphous powder that is odorless and decomposes with liquefaction at 225 C. For clinical use it is supplied in 5 mg. compressed tablets that are scored so that they may be easily broken in half.

The value of cortisone and corticotropin in the therapeutic management of pemphigus vulgaris, systemic lupus erythematosus, exfoliative dermatitis, and atopic dermatitis has been demonstrated repeatedly. It is also a well-known fact that when these drugs are used in the treatment of the afore-mentioned conditions only temporary remission is obtained. If the dose of these steroids is reduced below the level of the established maintenance dose, symptoms recur. This study was conducted to determine the value of these new synthetic steroids in the treatment of selected dermatoses.

From the Division of Dermatology, Department of Medicine, University of Maryland School of Medicine.

The prednisone used in this study was supplied as Meticorten by the Schering Corporation, Bloomfield, N. J.

1. Bunim, J. J.; Pechet, M. M., and Bollet, A. J.: Studies on Metacortandralone and Metacortandracin in Rheumatoid Arthritis: Antirheumatic Potency, Metabolic Effects, and Hormonal Properties, J. A. M. A. **157**: 311-318 (Jan. 22) 1955.

METHOD

The patients included in this investigation were admitted to the University Hospital for diagnostic survey and institution of treatment. In all instances the diagnoses were confirmed by biopsy prior to the institution of therapy with prednisone. Electrolyte studies, total eosinophil counts, and other routine laboratory procedures were also performed. Follow-up studies were instituted at periodic intervals following initiation of treatment with the new synthetic compound.

Procedure of Administration.—For the duration of treatment with prednisone all local applications and other systemic therapy were withheld. In each instance treatment was initiated with a total daily dose of 60 to 80 mg. divided into four equal parts administered every six hours. After improvement was noted, the original dose was maintained for two to three days and then gradually reduced by 5 mg. every three or four days until a maintenance dose was established. One infant, aged 3 years, was treated with an initial dose of 30 mg. of the steroid divided into four equal parts, and, after improvement was noted, the dose was reduced by 2.5 mg. every four days until the maintenance dose was established. No attempt was made to alter the sodium chloride intake in any patient in this series during the course of treatment.

Clinical Studies in Patients Who Had Received Steroid Therapy.—Five of the 11 patients included in this report had previously received systemic steroid therapy with either corticotropin, cortisone, or hydrocortisone (table 1). Involution of lesions was incomplete in all five at the time treatment with prednisone was initiated. None of these persons had been completely stabilized with a maintenance dose of the steroid with which they were being treated. Two of these individuals had acute disseminated lupus erythematosus, and in both of them the diagnosis had been established by biopsy and the presence of the L. E. cell phenomenon. The female, aged 48, had been receiving both cortisone and corticotropin for one and a half years but her illness was incompletely controlled. Periodic relapses of the skin eruption, joint pains, and dyspnea necessitated frequent increases in the dose of corticotropin or cortisone. Prior to institution of prednisone therapy she had been receiving 30 units of corticotropin (Acthar) gel every other day, and, in spite of this, she had joint pains, dyspnea, persistent skin lesions, and a feeling of general weakness. Treatment was initiated with a total daily dose of 60 mg. of prednisone divided into four equal parts administered every six hours. Improvement was noted in one week, and, in three weeks, all cutaneous lesions had disappeared. It then was possible to reduce the dose of prednisone gradually to a maintenance dose of 20 mg. daily. Over a six week observation period, no relapses of cutaneous lesions occurred and a feeling of well-being persisted. The white male, aged 40, who had acute disseminated lupus erythematosus, improved while receiving treatment with cortisone, although a total daily dose of 150 mg. was required. Arthralgia and a feeling of depression persisted, and some active cutaneous lesions remained. A total daily dose of 60 mg. of prednisone divided into four equal parts was administered every six hours. One week later all skin lesions had subsided, the joint pains had

disappeared, and he had a feeling of general well-being. The dose was gradually reduced by 5 mg. every five days to a total daily dose of 15 mg. When this level had been reached, joint pains recurred, with erythema developing at the site of some of the original skin lesions. The dosage was increased to 20 mg. daily and all symptoms subsided. He has been receiving this maintenance dose for eight weeks prior to the time of writing, and no recurrence of symptoms has been noted. Both of these individuals state that the feeling of depression experienced while taking corticotropin or cortisone has not recurred since treatment was instituted with prednisone.

recurrence of symptoms. She has continued to receive a maintenance dose of 20 mg. daily for the two months prior to writing without noting any recurrence subjectively or objectively. Both of these patients have experienced a persistent feeling of well-being.

A young white male, aged 40, had exfoliative dermatitis of undetermined origin, and the condition was incompletely controlled with a dose of 80 mg. of hydrocortisone daily. At the time administration of prednisone was instituted, this patient had a generalized, diffuse, erythematous, scaling macular eruption. There was bilateral edema of the lower extremities, and the itch-

TABLE 1.—*Data on Patients Previously Treated with Steroids**

Case No.	Diagnosis	Age	Sex	Previous Steroid Therapy	Length of Steroid Therapy	Result of Previous Steroid Therapy	Maintenance Dose of Steroid	Initial Daily Dose of Prednisone	Results of Prednisone Therapy	Maintenance Dose of Prednisone
1	Pemphigus vulgaris	61	M	Corticotropin and cortisone	8 mo.	Partial improvement. New blebs continue to appear. Itching persisted	40 units corticotropin gel every other day	80 mg., 4 divided doses	Involution of all lesions. Cessation of itching	15 mg. daily, 3 divided doses
2	Pemphigus vulgaris	57	F	Corticotropin and cortisone	8 mo.	Partial improvement. New blebs continue to appear. Itching intense	40 units corticotropin gel every other day	80 mg., 4 divided doses	Involution of all lesions. Cessation of itching	20 mg. daily, 4 divided doses
3	Acute disseminated lupus erythematosus	40	M	Cortisone	5 mo.	Active skin lesions and slight joint pains persist	150 mg. cortisone daily	60 mg., divided into 4 equal doses	Involution of all lesions, and disappearance of joint pains	20 mg. daily, divided into 4 equal doses
4	Acute disseminated lupus erythematosus	48	F	Cortisone and corticotropin	1½ yr.	Some skin lesions. Persistent weakness and dyspnea	30 units corticotropin gel every other day	60 mg., divided into 4 equal doses	Involution of all lesions. General feeling of well-being	20 mg. daily, divided into 4 equal doses
5	Exfoliative dermatitis, postmedication	40	M	Hydrocortisone	6 wk.	Edema of extremities persistent. No relief from itching. No involution of lesions	50 mg. hydrocortisone daily	60 mg., divided into 4 equal doses	Improvement in eruption in 48 hr. Eventual involution of lesions occurred	20 mg. daily, divided into 4 equal doses

* All patients in this group were Caucasian.

TABLE 2.—*Data on Patients Previously Untreated with Steroids*

Case No.	Diagnosis	Age	Race	Sex	Initial Total Dose of Prednisone, Mg./Day	Time Improvement Appeared, Days	Time Involution of Lesions Complete, Days	Total Maintenance Dose of Prednisone, Mg./Day	Adverse Effects
1	Atopic dermatitis	3	W	F	30	5	14	7.5	.....
2	Atopic dermatitis	23	W	F	60	7	21	20	Slight gain in weight
3	Atopic dermatitis	41	W	F	60	7	14	15	.....
4	Atopic dermatitis	38	W	M	60	7	21	15	.....
5	Exfoliative dermatitis	40	N	F	60	8	21	15	.....
6	Exfoliative dermatitis	43	W	M	60	5	14	15	Slight feeling of gastric fulness

In two patients with pemphigus vulgaris control was incomplete with the use of corticotropin or cortisone. At the time of initiation of treatment with prednisone, both of these patients were receiving 40 units of corticotropin gel every other day, and, in spite of this, subjective symptoms of severe itching persisted and new blebs continued to appear. In both of these individuals treatment was initiated with 80 mg. of prednisone divided into four equal parts and administered every six hours. Seven days after initiation of treatment with this compound all cutaneous lesions had disappeared and itching had subsided. The dose of synthetic steroid was gradually reduced by 5 mg. every five days until a maintenance dose had been established. The male patient remained free of symptoms for a two month period with a maintenance dose of 15 mg. daily, but in the female patient it was impossible to reduce the dose below 20 mg. without noting

ing was intense. Treatment was initiated with a total daily dose of 60 mg. of prednisone divided into four equal parts administered every six hours. Marked improvement was noted in 48 hours. There was complete involution of all lesions in 14 days, and it was then possible to reduce the dose of the synthetic steroid by 5 mg. every fourth day until a maintenance dose of 20 mg. daily was established.

Clinical Studies in Patients Who Had Not Received Steroid Therapy.—Six of the patients in this series had not received systemic steroid therapy prior to the administration of prednisone (table 2). Two of these individuals had exfoliative dermatitis that had been resistant to all other forms of treatment, and four had severe generalized atopic dermatitis. The two patients with exfoliative dermatitis of undetermined origin were treated with an initial daily dose of 60 mg. of prednisone divided into four equal parts administered every six hours. Improve-

ment was noted in both individuals in 5 and 8 days, respectively, and in 14 and 21 days, respectively, complete involution of lesions had been noted. In both of these individuals the dose was gradually reduced by 5 mg. every four to five days until a maintenance dose of 15 mg. had been established.

Of the four patients who had atopic dermatitis, one was an infant, aged 3, in whom the initial dose of prednisone was 30 mg. daily divided into four parts. Marked improvement was noted in 5 days, and in 14 days involution of lesions was complete. It was possible to reduce the dose by 2.5 mg. every four days until a maintenance dose of 7.5 mg. had been established. On continued observation over a longer period of time, it will probably be possible to reduce this dose still further. The remaining three patients with atopic dermatitis were adults; treatment was initiated in all three with a total daily dose of 60 mg. of prednisone divided into four equal doses administered every six hours. Improvement was noted in all of them within 7 days, and in from 14 to 21 days involution of lesions was complete. It was possible to reduce the dose of prednisone gradually every four or five days by 5 mg. to reach a maintenance dose of 15 mg. daily in two individuals and 20 mg. daily in the remaining one.

SIDE-EFFECTS

No serious side-effects were noted. No change was made in the eating habits of any of these individuals, and no attempt was made to reduce the sodium chloride intake prior to institution of treatment with prednisone. All of these patients noted an increase in appetite, but none of them gained weight. The male patient who had acute disseminated lupus erythematosus noted slight epigastric discomfort during the first three days of treatment, but this was transitory. At the time of this report it has not been possible to completely withdraw the administration of prednisone without producing relapses of the original lesions. Rounded facies were not noted as a complicating feature, and none of the patients developed peripheral edema.

LABORATORY STUDIES

Blood Picture.—No significant change was noted in the blood picture in any of the 11 patients. In those six individuals previously untreated with steroids, there was a prompt significant fall in the total eosinophil count following initiation of the synthetic steroid. When the prednisone was withdrawn, the total eosinophil count returned to normal, and, when the drug was readministered, it promptly fell again.

Electrolyte Studies.—No significant alteration was noted in the blood sodium, potassium, or nitrogen levels during the course of prednisone therapy in any of these patients. No change was noted in the albumin-globulin ratio in any of these individuals during the course of treatment. None of the patients developed glucosuria, and the blood glucose levels remained stabilized.

COMMENT

This preliminary report indicates that prednisone has therapeutic value in pemphigus vulgaris, atopic dermatitis, acute disseminated lupus erythematosus, and exfoliative dermatitis. One of its major virtues is the lack of serious side-effects noted on prolonged administration. As Bunim and his co-workers stated [1]: "It is reasonable to expect withdrawal symptoms after prolonged administration of these new steroids, since, they, like their antecedent suppress the manifestations of the disease and endogenous cortical steroid production." It is possible that with a larger group of patients some of the serious side-effects noted with cortisone and corticotropin administration may become apparent. The results of these studies indicate that these synthetic steroids are four or five times as potent as cortisone or hydrocortisone without the severity or frequency of side-effects. Five of the patients in this series who failed to respond to cortisone or corticortropin have responded promptly to the administration of prednisone. Preliminary studies in 40 patients indicate that both prednisolone and prednisone are also of value in the local treatment of some selected dermatoses. Prednisone possesses the greater efficacy.

SUMMARY AND CONCLUSIONS

Prednisone is a synthetic steroid that apparently possesses the physiological activity of an adrenal cortical hormone. There is a significant decrease in the total number of circulating eosinophils following the administration of this drug. It is an effective anti-inflammatory agent. Subjective and objective improvement have been noted in the treatment of acute disseminated lupus erythematosus, pemphigus vulgaris, exfoliative dermatitis, and atopic dermatitis. Prednisone is apparently from four to five times as active in these conditions as cortisone, hydrocortisone, or corticotropin, without producing more frequent or severe undesirable side-effects. Laboratory studies in the series of patients studied indicated no sodium retention and no loss of potassium or nitrogen. The albumin-globulin ratio showed no significant change in any of the patients studied. None of the individuals in this series developed glycosuria. After initial improvement was noted, it was possible to reduce the dose of the synthetic steroid gradually to a maintenance dose. When the dose was reduced below the level of this maintenance dose, symptoms recurred in all of the individuals. More extensive studies are indicated to determine the therapeutic range of this compound.

Cough.—The simplest efficient method of management [of cough] is desirable but not a substitute for a knowledge of the cause and effect. This is even more important when it is realized that 13 per cent of the population of this country will be over sixty-five years of age at the end of this century. Of this 13 per cent, it is estimated that 6 per cent will be "chronic coughers" as a result of many chronic lung diseases. An example is the increase of hypertrophic emphysema, or consider the coughing in bronchiectasis which "is the second commonest lung disease. The National Health Survey of 1935-1936 showed 1,700,000 persons to be affected by chronic bronchitis. To these cases many of the 1,150,000 persons with chronic sinusitis can be added, since chronic bronchitis and sinusitis frequently complicate each other. Furthermore, most cases of chronic asthma, although still indexed among the 3,500,000 victims of hay fever and asthma, represent the nonallergic infectious type of asthma rather than true allergy. This survey would then indicate that in this country alone, at least 2 to 3 million persons suffer from chronic bronchopulmonary disease."—A. Worth Hobby, M.D., Cough, Its Pathology and Management, *The American Journal of Surgery*, February, 1955.

HYDROCORTISONE TERTIARY-BUTYL-ACETATE BY INTRA-ARTICULAR INJECTION

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Ralph A. Jessar, M.D.
Louis Udell, M.D.
Nathan M. Smukler, M.D.
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In 1951 we reported the effectiveness of the intra-articular injection of hydrocortisone acetate in the local management of arthritic inflammation.[1] Nearly a hundred supplementary and confirming reports have appeared subsequently in both the American and the foreign medical literature, showing that this adjuvant to treatment of joint disease has now been widely accepted here and abroad.[2] During the past three and a half years we have performed more than 17,000 intrasynovial injections of hydrocortisone acetate into the joints, bursae, or tendon sheaths of nearly 1,300 patients for various forms of rheumatic disease. In about 80% of instances, the injection was followed by at least a brief period of improvement of symptoms [3]; however, the effect was so minimal or transitory in about one-third of our cases that it proved useless as practical treatment for the local condition. Because of this finding, a search has been made for preparations or agents capable of prolonging the local palliative effect of hydrocortisone.

We had found [4] that hydrocortisone acetate injected into the joint cavity was largely absorbed by the lining tissue of the synovial membrane, apparently without splitting the ester, whereas the unabsorbed residue was rapidly hydrolyzed in the synovial fluid. Could this mean that higher, less soluble esters of hydrocortisone, likewise absorbed unchanged by the synovial membrane, might be more slowly utilized by the inflamed synovial tissue, thus prolonging the effect? We used a sterile, microcrystalline suspension of such a higher, less soluble hydrocortisone ester, hydrocortisone *t*-butylacetate, the first higher ester of hydrocortisone assayed.

From the Arthritis Section, Department of Medicine, Hospital of the University of Pennsylvania.

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The hydrocortisone tertiary-butylacetate used in this study was supplied by Merck & Company, Inc., Rahway, N. J.

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METHOD

The manner of testing the unknown preparation for relative anti-inflammatory effectiveness was by simple clinical trial. The clinical material consisted of 92 patients with rheumatoid arthritis and 79 patients with osteoarthritis of one or both knees who had previously received intra-articular injections of hydrocortisone acetate into the affected knees as part of their treatment. No change was made in the systemic therapy or general supportive measures during the period of comparison. Since the newer ester appeared identical with hydrocortisone acetate in the syringe, it was easy to preclude any knowledge of substitution from the patients, so that the psychological effect of "new treatment" was eliminated from the study. Identical doses of hydrocortisone acetate and hydrocortisone *t*-butylacetate were always used in the comparison.

Follow-up examinations were made on each patient after injections to determine the degree of ameliorative effect from the injection and the duration of the amelioration. In every case in which the comparative effects from the acetate and butylacetate were equivocal, subsequent injections alternating between the two preparations were carried out. In a few patients in whom both knees were about equally involved, simultaneous comparison of effect was possible by injecting hydrocortisone acetate into one knee and the *t*-butylacetate into the other.

Records included specific data concerning the degree of improvement in swelling, tenderness, freedom of motion, and degree of relief from pain on weight bearing after each injection. Also recorded was the duration of the relief from onset until the patient noted definite return of symptoms. This was aided by a simple diary kept by each patient and brought with him to each follow up visit. Subsequent injections were never given until the joint had returned to its pretreatment state, so that cumulative effects were avoided. For the same reason injections were never repeated oftener than every two weeks, even though the effect had been minimal and transient.

RESULTS

As had been previously noted [3] after injection of hydrocortisone acetate, the intra-articular instillation of hydrocortisone *t*-butylacetate produced widely divergent results among patients in the series of 171 cases. Seven patients exhibited no benefit whatever from the newer ester, even though the standard preparation produced consistent palliation each time it was injected. At the opposite extreme were nine patients who had previously experienced little or no relief following hydrocortisone acetate instillation in whom a marked amelioration persisting many weeks was noted after injection of hydrocortisone *t*-butylacetate into the same joint. In about 90% of cases, however, the difference in effectiveness between the preparations of the hormone was not as marked.

Results are summarized in the table. If injections of hydrocortisone *t*-butylacetate into the joint produced an unequivocal increase in degree of benefit as compared with that resulting from hydrocortisone acetate, that patient was included in the group "F *t*-BA superior to FA." Likewise, if the duration of effectiveness in days was clearly longer after instillation of the newer ester as compared with the standard "F" acetate, that patient was included in the appropriate space in the first column. The patients listed in the second column showed no definite difference between effects from the two preparations, and in the last column are those patients in whom the acetate ester produced greater benefit. A majority of patients were found to experience greater and longer effect from hydrocortisone *t*-butylacetate. When results were considered by diagnosis, it was found that a higher percentage of patients with rheumatoid arthritis experienced greater palliation from the new ester, but a higher percentage of those with osteoarthritis achieved a longer lasting effect from "F *t*-BA." It is questionable, however, that these differences are significant.

Effectiveness of Intra-Articular Injections of Hydrocortisone Acetate as Compared with Hydrocortisone Tertiary Butylacetate

Disease	No. of Cases	F t-BA * Superior		F t-BA = FA †		FA Superior	
		No.	%	No.	%	No.	%
A. Comparison by Degree of Amelioration from Injection							
Rheumatoid arthritis	92	62	67	26	28	4	5
Osteoarthritis	79	49	62	25	32	5	6
Total cases	171	111	65	51	30	9	5
B. Comparison by Duration of Amelioration from Injection							
Rheumatoid arthritis	92	49	53	36	39	7	8
Osteoarthritis	79	52	66	23	29	4	5
Total cases	171	101	59	59	35	11	6

* Hydrocortisone tertiary-butylacetate.
† Hydrocortisone acetate.

Duration of effectiveness from an injection was more easily quantitated than the degree of effect, and it is significant that the percentage of patients experiencing longer effect from *t*-butylacetate injection was less than for those estimated to have achieved greater palliation. This would indicate that the duration of effectiveness is the more critical measurement to be considered in the comparison. This is particularly emphasized when it is noted that only those patients in whom the hydrocortisone *t*-BA was followed by a relief period of three days or more in excess of that which followed injection of "F" acetate were included in the group "F *t*-BA superior to FA." In over half of this group the period of relief following the "F *t*-BA" injection was increased 2 to 10 times over that following injection of a like amount of the hydrocortisone acetate.

By the simple method of adding together the total days of relief of symptoms in all 171 cases following hydrocortisone-*t*-butylacetate injection and dividing by 171 we found the average duration of relief was 16 days, whereas similar data after hydrocortisone acetate injection gave an average of slightly less than 9 days. Therefore, the "duration ratio" of the newer ester, as compared with the acetate, was almost 2:1. The onset of relief following injection of the hydrocortisone *t*-butylacetate averaged 18 hours after injection, whereas hydrocortisone acetate injection on the average produced detectable relief of symptoms within 14 hours. The incidence of exacerbation of joint symptoms following injection in this series was three from "F *t*-BA" and four following "FA." No other complications were encountered.

CONCLUSIONS

From a clinical comparison of relative anti-arthritic effectiveness of identical doses of hydrocortisone acetate and hydrocortisone tertiary butylacetate intra-articularly injected, it appears that in about 60% of 171 cases of either rheumatoid arthritis or osteoarthritis the tertiary butylacetate ester of hydrocortisone produced a greater and longer-lasting period of palliation. In about 35% of the cases there was no appreciable difference in effect from the two preparations of the hormone, and, in about 5%, the hydrocortisone acetate was superior in effectiveness.

Because of the variation in individual responsiveness in favor of one ester or the other, it is doubtful that the hydrocortisone *t*-butylacetate will ever completely supersede hydrocortisone acetate for intra-articular use, but it will find its main indication for intra-articular injection in those patients found refractory to the older preparation. The results are in no way spectacular and indicate only that the way is open to finding more effective and longer-acting preparations of hydrocortisone for intra-articular use.

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Air Pollution.—With the growth of population and industry, air pollution problems have become more numerous and present an increasing hazard to public health. Our knowledge of the chronic effects is too meager to justify a complacent attitude. Although great advances have been made in the last five years in the development of instruments and technics for the measurement of various air contaminants, there has been little, if any, progress in the elucidation of the causes of acute symptoms leading to fatal effects in air pollution disasters. Progress in evaluating the extent of chronic effects or in proving the existence of this type of injury to health in industrial communities has been virtually nil. Our experience is still confined to indoor exposures in industrial atmospheres, occupational diseases, and knowledge acquired in industrial hygiene and medical practice. The Detroit River area health study represents a scientific attempt to determine the effects of prolonged exposure to such contaminants as occur in the atmosphere of a highly industrialized region. The approach is not a rigid one and methods will be improved as dictated by experience. The findings will be of value to other industrial communities and provide guidance to those who are able to undertake elsewhere similar investigations in the field of public health.—M. Katz, Ph.D., Atmospheric Pollution: A Growing Problem in Public Health, *American Journal of Public Health*, March, 1955.

SPLENIC HEMORRHAGE FOLLOWING PERCUTANEOUS SPLENOPORTOGRAPHY

Telfer B. Reynolds, M.D.
William Mikkelsen, M.D.
and
Allan G. Redeker, M.D., Los Angeles

Roentgen visualization of the portal venous system by the percutaneous injection of radiopaque material into the spleen was reported in the European literature in 1951.[1] Numerous subequent reports from Europe, North Africa, and South America indicated that the technique was being widely employed, and six references in English that described the results of the procedure in a total of 61 patients[2] were also found. The possibility of splenic hemorrhage has been recognized by all authors, but this complication appears to have occurred infrequently. Only small amounts of blood were found in the peritoneal cavities of those patients who underwent laparotomy after the injection,[3] although Cooper and others describe one patient who developed signs of shock a few hours after the splenic puncture and required transfusion.[2f] Walker and others injected iodopyracet (Diodone) percutaneously into a normal spleen during a laparotomy, and the patient developed signs of splenic hemorrhage three days later for which splenectomy was required.[2b] In 12 subsequent splenoportograms they encountered no evidence of serious bleeding. No other complications were mentioned in the six reports.

Though we have recognized the value of splenoportography in instances of portal hypertension and have noted the absence of serious complications in the reported cases referred to above, we nevertheless have been reluctant to use this procedure, unless important information was anticipated. For this reason, the procedure was employed by us in only three instances. The first two were in patients with extrahepatic portal hypertension; a splenoportogram was performed on the first immediately before scheduled laparotomy, and on the second during laparotomy. In the first patient, a significant subcapsular hematoma measuring about 10 by 6 cm. was observed when the abdomen was opened one hour after the percutaneous splenoportogram had been done. The second splenoportogram was performed on the operating table with the abdomen open. In this instance, brisk bleeding occurred, which was controlled by pressure. In both instances, splenectomy was performed as a definitive procedure for the portal hypertension, which, in each case, was due to splenic vein obstruction. The third splenoportogram that we performed resulted in serious hemorrhage necessitating splenectomy. Because of this complication, we believe that the procedure is more hazardous than the initial reports indicate.

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3. Dreyer and Budtz-Olsen.[2a] Bahnson and others.[2c] Cooper and others.[2f]

REPORT OF A CASE

A 32-year-old woman, complaining of weakness of one month's duration, was found to have hepatosplenomegaly. A sharp, nontender liver edge and a firm spleen were palpable, 5 and 2 in., respectively, below the costal margins. There was no lymphadenopathy. Normal values were obtained for serum protein levels, sulfobromophthalein (Bromsulphalein) sodium retention, and prothrombin time. A severe microcytic hypochromic anemia was present, which seemed adequately explained by persistent menometrorrhagia. The clotting time was slightly prolonged, but there was no bruising; the bleeding time was normal, and adequate numbers of platelets were visible on a blood smear. Hysterectomy was performed, revealing uterine leiomyomas, an enlarged spleen, and predominant enlargement of the right lobe of the liver, which had a smooth surface. A wedge biopsy of the liver failed to show any hepatocellular abnormalities or any fibrosis; however, the sinusoids and hepatic and portal venous channels appeared to be unusually large throughout the specimen. Portal venography was decided upon because of the suspicion of vascular disease of an angiomatous type in the liver. It was thought that the associated splenomegaly might be a result of portal hypertension. After local infiltration with procaine, a no. 18 gauge, 3 in. spinal needle was inserted through the abdominal wall below the rib cage into the splenic substance. Red blood was aspirated at this point. Thirty cubic centimeters of sodium acetrizoate 70% (Urokon) was then injected rapidly, requiring about nine seconds, and several exposures were made. The intrahepatic portal vein radicles were well visualized and appeared normal. The patient held her breath satisfactorily during the splenic puncture and injection. Manual pressure on the abdominal wall in the splenic area was maintained for 10 minutes after the needle removal, and she remained flat in bed. Within an hour, she began to complain of pain in the left shoulder tip and distress in the left upper quadrant of the abdomen. Over the course of the next eight hours, the shoulder pain continued, left upper quadrant tenderness remained, the abdomen became distended, and there developed evidence of fluid in the flanks. The hemoglobin level dropped 1.5 gm. per 100 cc., and the pulse rate increased from 90 to 130 per minute in spite of the administration of 1,000 cc. of whole blood.

Operation was decided on 12 hours after the initial procedure. Approximately 1,500 cc. of liquid blood was found in the peritoneal cavity. The intestine was distended. There was a large hematoma distending the capsule of the spleen over its entire outer surface, and blood was oozing slowly from a small 3 to 4 mm. needle rent in the lower pole. The liver remained as previously described, and mesenteric vein pressure was normal. A splenectomy was performed from which the patient recovered satisfactorily. The spleen weighed 740 gm. (including the hematoma), but its microscopic structure was not remarkable. An abdominal lymph node removed at the time of surgery failed to reveal any abnormalities. At the present time, the patient's symptoms are minimal, the hepatomegaly persists, and its etiology remains obscure.

CONCLUSIONS

Roentgen visualization of the portal venous bed is of unquestioned value in certain instances, particularly if extrahepatic portal hypertension is suspected; however, if the radiopaque substance is injected into the spleen, hemorrhage may result. Facilities for splenectomy must be available.

1200 N. State St. (33) (Dr. Reynolds).

V 1
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A SIMPLE CALCULATOR FOR DIRECT CONVERSION OF CHEMICAL VALUES

INTERCONVERSION OF MILLIEQUIVALENTS PER LITER WITH MILLIGRAMS PER HUNDRED CUBIC CENTIMETERS AND VOLUMES PER CENT

Charles A. Sarnoff, M.D., Jamaica, N. Y.

The importance of fluid and electrolyte balance studies in modern medicine cannot be overestimated. In almost all fields of medicine, some application of the principles of this science is known. Calculations and imbalances are most satisfactorily worked out in milliequivalents per liter. Unfortunately, laboratory results are most often reported in volumes per cent and milligrams per 100 cc. To convert these values to milliequivalents per liter requires much time and effort. A simple modification of an ordinary slide rule that can be effected in a few minutes facilitates the conversion to such an extent that what once took arduous hours can be done in seconds. The calculator is an ordinary slide rule or two opposed logarithmic scales (logarithmic graph paper will do) with marks made on the D scale so that, when the number 1 on the C scale is opposed to a mark, the C scale is related to the D scale as the ratio of milliequivalents per liter to milligrams per 100 cc. or volumes per cent of the ion designated by the mark.

CONSTRUCTION OF CALCULATOR

On an ordinary slide rule, make marks on the D scale at:

20 for calcium
22.2 for carbon dioxide
23.1 for sodium
39 for potassium
58.3 for chloride

The value reported for sodium chloride by the laboratory is treated as the value for chloride ion for the purposes of this calculation, since the value in milliequivalents per liter of chloride in sodium chloride equals that of the sodium chloride.

Should one wish to set up a rule for a specific ion not included in the five mentioned above, one may derive the number opposite which the mark is to be placed by using the following rules, which were used to derive the values mentioned above. 1. Select any arbitrary value in milligrams per 100 cc. or volumes per cent for the ion in question (e. g., 60 vol. % of carbon dioxide). 2. Using the formula

$$\text{mEq./liter} = \frac{\text{mg./100 cc.} \times 10 \times \text{valence}}{\text{atomic weight}}$$

or

$$\text{mEq./liter} = \frac{\text{Vol. \%} \times 10}{22.4}$$

calculate the value in milliequivalents per liter equal to the arbitrary value selected in step 1 for the ion in question (i. e., 60 vol. % of carbon dioxide equals 27 mEq. per liter). 3. Find the arbitrary value for the ion in milligrams per 100 cc. or volumes per cent on the D scale and set it opposite the calculated equivalent value in milliequivalents per liter on the C scale (i. e., 60 on the D scale opposite 27 on the C scale). 4. The index line (number 1 on the C scale) is now opposite the desired mark on the D scale (i. e., 22.2). 5. Henceforth, any interconversion related to the ion in question can be done simply by placing the index line (No. 1) on the C scale opposite the mark and reading the values directly from the rule.

USE OF CALCULATOR

Place the index line of the C scale opposite the mark on the D scale that represents the ion whose equivalent value is to be found. Any value on the C scale is the converted value of that ion in milliequivalents per liter from the value in milligrams per 100 cc. and volumes per cent on the D scale that appears directly opposite it. For example, for carbon dioxide, set 1 on the C scale opposite 22.2 on the D scale. If one arbitrarily selects the value 60 vol. % on the D scale, directly opposite this value on the C scale one reads the converted value, 27 mEq. per liter. Selecting another arbitrary value, 66.6 vol. % of carbon dioxide, one finds directly opposite it on the C scale the converted value for carbon dioxide of 30 mEq. per liter. In this way, 10 or 15 calculations can be done in about 45 seconds.

185-47 80th Rd. (32).

DIAGNOSTIC PROBLEMS

PRESENTATION OF CASE

Frederick D. Dallenbach, M.D., Chicago

A 48-year-old man complained of cramping infraumbilical pain of four weeks' duration, pain in the right side of his chest and precordial pain experienced at times during exercise, and a weight loss of 10 lb. (4.5 kg.). For the previous 25 years he had taken calcium powders, presumably for a peptic ulcer. He had had an appendectomy and two hemorrhoidectomies, but there was occasional spotting of bright red blood rectally. He had had gonorrhea and painless jaundice for one month nine years before admission. About two months prior to admission his blood pressure was 122/78 mm. Hg. His heart was found to be enlarged to the left. Hemorrhoids were found, but a proctoscopic examination was otherwise normal. The serologic test for syphilis was negative, and his blood cell counts were within normal limits. Roentgenograms showed diffuse dilatation of the aorta, a superficial duodenal ulcer, and spasm of the sigmoid colon. He was placed on a low residue diet with antacids. For the next two months he progressed well but was admitted to the hospital in shock, complaining of a severe sudden cramping pain in the right lower portion of his chest of five hours' duration that radiated to his right shoulder.

Physical Examination.—The patient was cyanotic and in severe pain. His blood pressure was 60/40 mm. Hg, rising to 110/70 mm. Hg in a few hours. The lungs were resonant. Questionable rales were heard in the lower lobe of the left lung. A pleural friction rub was audible at the base of the right lung. Pressure on his abdomen elicited pain in his right shoulder.

From the Department of Pathology, University of Illinois.

Laboratory Findings.—The hemoglobin level was 14.5 gm. per 100 cc., and the leukocyte count was 21,300 per cubic millimeter, with 87% neutrophils. The sedimentation rate was 28. Initially the patients' icterus index was 11, but it fell to 4. The albumin-globulin ratio was 3.7 to 1.9 gm.; the serum nonprotein nitrogen level was 33 mg. per 100 cc.; the glucose level 98 gm. per 100 cc.; and the whole blood chloride level 519 mg. per 100 cc. The blood Wassermann reaction was negative. A roentgenogram of his chest showed elevation of the right leaf of the diaphragm.

Course.—The day following admission the patient coughed up blood-tinged sputum. Sulfadiazine was prescribed. In the next week he had several episodes of sudden severe pain in the right lower portion of his chest. Although his temperature and pulse remained slightly

Aneurysm of lower thoracic aorta with bilaterally attached diaphragm. Heart, upper left.

elevated, the leukocyte count fell to 7,800 per cubic millimeter. An effusion, confirmed by roentgenograms, was detected in the right side of his chest. On aspiration a bloody fluid was obtained containing no bacteria and a few leukocytes. The patient improved slowly and was discharged after six weeks. Six months later he was readmitted complaining of bilateral chest pain radiating into the epigastrium and back. A mass was disclosed in the posterior mediastinum, displacing the esophagus forward. No gastric, duodenal, or urinary lesions were found. The severe pain continued, and because of opiate addiction a paravertebral block was done. Shortly thereafter the patient had a sudden severe pain in his left shoulder, and a left hemothorax and hemopericardium were found. Although the pain was difficult to control, he gradually improved and was discharged after two months. Six months later he returned, still complaining of thoracic pain, to which difficulty in swallowing was added. He had lost 30 lb. (13.6 kg.). The veins of all extremities were prominent. During studies to determine circulation time he suddenly retched, vomited violently copious amounts of bright blood, and complained of severe thoracic chest pain. He died soon afterward.

ANATOMIC DIAGNOSIS

The right pleural cavity was obliterated by fibrous adhesions, especially dense posteroinferiorly. A fibrous layer 2 cm. thick covered the lower thoracic vertebrae. The left pleural space contained 2,500 cc. of fresh, partially clotted blood. The heart weighed 250 gm. and was displaced sharply to the right by an aneurysm of the thoracic aorta measuring 13 by 17 by 15 cm. descending to the diaphragm and projecting mainly to the left. The aortic valve was normal, as were the coronary ostiums. The ascending aorta was thickened and the intima heavily wrinkled and spotted by numerous roughened plaques and distorted by arteriosclerotic changes. The aneurysm had partially eroded the right side of the 9th and 10th thoracic vertebrae and was freed with great difficulty from the dense adhesions. This was considered the site of previous perforation, and the adhesions were believed to be due to old organized blood clot. The sac protruding to the left and anteriorly was thin walled and covered by a thin layer of diaphragmatic muscle. In the central posterior portion the wall was hemorrhagic and a ragged perforation measuring 3 by 7 mm. was seen. This defect was considered as the source of the hemothorax. The aneurysmal pouch here was partially filled with an antemortem thrombus and partially with fresh blood clot. The lining of the abdominal aorta was greatly thickened and altered by numerous yellow-gray plaques and ulcers.

The esophagus was abruptly displaced to the left and was firmly adherent over the left anterior border of the aneurysm. The medial esophageal wall was necrotic and was eroded over a distance of 5 cm. where the sac was most prominent. The esophageal lumen communicated freely with the aneurysm. The stomach and small intestine were filled with partially clotted blood. Microscopic studies of the ascending aorta and aneurysm revealed a mesaortitis with adventitial fibrosis and an inflammatory infiltrate consistent with a syphilitic process. There were marked intimal atherosclerotic changes as well.

COMMENT

Norman Roberg, M.D., Chicago

This patient's illness emphasizes several features of syphilitic aortitis with aneurysm: (1) recurrent episodes of bleeding, (2) the appearance of signs and symptoms late in the course of aneurysms of the descending thoracic aorta, (3) the relationship between syphilis and atherosclerosis of the aorta, and (4) the inconstancy of a positive serologic test for syphilis in the presence of active syphilitic disease.

The first definitive hemorrhage occurred 15 months before death. The sudden onset of shock, with intense pain in the right side of the chest, is more consistent with rupture of the aorta than with inflammation of the lung

From the Department of Medicine, University of Illinois.

and pleura. Though aneurysms of the descending thoracic aorta may compress the major bronchi, with consequent atelectasis, pneumonitis, and bronchiectasis ("aneurysmal phthisis"), this patient's hemoptysis more likely was due to "aneurysmal weeping" into the lung. The normal proportion of hemoglobin on admission would be consistent with either a hemorrhage of small volume or a delay in compensatory hemodilution because of the state of shock. Marked leukocytosis is common with hemorrhage into the spaces or tissues of the body. Transient elevation of the icterus index is common in pulmonary infarction, lobar pneumonia, and internal hemorrhage: bilirubin from the hemolyzing blood is presented to the liver in greater amounts than the liver can excrete. Not only is a large amount of bilirubin delivered to the liver, but in these severe illnesses it is probable that the hepatic excretory function is temporarily impaired.

The second hemorrhage occurred seven months later, shortly after an attempted paravertebral nerve blocking. This bleeding was into the left pleural cavity. Inasmuch as the aneurysm did not involve the ascending aorta within the pericardial reflection, and since no adhesions of the aneurysm to the pericardium were found at autopsy, the clinical diagnosis of hemopericardium was probably erroneous.

The third and fatal hemorrhage came after another eight months. At autopsy there were two perforations: one into the left pleural cavity and the other a free communication with the esophagus. The esophagus, normally being bound to the descending aorta, follows any distortion of the aorta. The distortion of the esophagus secondary to senile or atherosclerotic elongations or ectasias of the aorta is mild and asymptomatic. With syphilitic aneurysms of the aorta, displacement of the esophagus may be marked and dysphagia is common. Perforation of the aneurysm into the esophagus occurs only in a minority of the patients having dysphagia. Since this patient's terminal hemorrhage was heralded by severe retching and vomiting, it is suggested that the rupture may have been from the esophagus into the weak aneurysmal wall of the aorta. The normal esophagus can be ruptured by violent retching.

Death during the first rupture of an aortic aneurysm is the rule. This case emphasizes, however, the established exceptions of syphilitic, atherosclerotic, and dissecting aneurysms causing intermittent symptoms and signs of rupture or hemorrhage for months, rarely for years, before death.

This huge aneurysm had an approximate volume of 2 liters at autopsy, and must have been larger during life. Aneurysms localized to the descending thoracic aorta are the least common and the most silent clinically. Pain is their hallmark. The exertional thoracic pain suffered by this patient at the onset of his illness probably was not related to coronary artery insufficiency; the aortic ring and valves and the coronary arteries and their ostiums were normal. The pain was more likely the result of pressure on the spine by the aneurysm. The initial and transient distress below the navel, causing a 10 lb. weight loss in four weeks, is typical of neither duodenal ulcer nor a spastic sigmoid. Though the erosions were confined to the bodies of the 9th and 10th thoracic vertebrae, the proximity of these vertebrae to the 10th, 11th, and 12th thoracic nerve roots, which carry sensations from the hypogastrium, suggests that the low abdominal distress may have been radicular in nature. In vascular and local spinal disease, radicular pain is often mistakenly believed to originate from intrathoracic or intra-abdominal organs. Osler discussed the root pains of syphilitic aneurysm but emphasized the more common "deep-seated, boring, intense agony only relieved by maximum doses of morphine." This was, probably, the type of local pressure pain suffered by the patient during his latter months.

Moderate enlargements of the descending thoracic aorta, asymptomatic and harmless, are common in elderly persons with aortic atherosclerosis and occur in middle age under the accelerating influence of diastolic hypertension. Large and irregular aneurysms, associated with symptoms or signs of pressure, are either syphilitic or dissecting aneurysms. Syphilitic aortitis is usually most intense in the ascending aorta, with the degree of injury diminishing until the celiac axis of the abdominal aorta is reached. Beyond the celiac axis, significant syphilitic aortitis is rare. Atherosclerosis of the aorta is just the opposite in its sites of predilection: atherosclerotic changes in the aorta are least in the ascending aorta and increase as the aorta descends, being most marked in the lowest abdominal portion. The areas of the aorta injured by syphilis are especially susceptible to atheromatous disease. For this reason, syphilitic aortitis of a degree resulting in dilatation will usually show advanced atherosclerosis in the same area. On casual inspection the disease may be ascribed to atherosclerosis and the underlying syphilitic aortitis be unrecognized. It is this concomitant atherosclerosis that causes the almost pathognomonic calcification of the ascending aorta seen in the roentgenogram in syphilitic aortitis.

The clinical features of syphilitic and atherosclerotic disease of the aorta remain important. As this case illustrates, the standard serologic tests for syphilis are negative in about 20% of patients with syphilitic aortitis. This negativity may be present in patients below the age of 40 who have active aortitis and have not received specific treatment. Aortitis is the commonest visceral manifestation of syphilis. Now that visceral syphilis is becoming less common and physicians are less alert to its possible presence, there is special danger of not recognizing a potentially treatable disease when the serologic tests for syphilis are negative. Conversely, there is an increasing awareness of the many biological false positive tests. Most of these false positive tests result from a variety of infections, commonly from viral hepatitis and infectious mononucleosis. In other patients, a false positive test is the first evidence of such diseases as disseminated lupus erythematosus.

Recognizing that the Kahn, Wassermann, and other serologic tests may be negative in syphilitic aortitis and may be positive in patients not having syphilis, dependence on these nonspecific tests is dangerous. It is hoped that the future wider use of the treponemal immobilizing test will obviate many of these difficulties. Early syphilitic aortitis may be arrested by penicillin therapy. Localized aneurysms may be resected surgically. Syphilitic aortitis is not, and will not soon become, a museum disease of the past.

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WANTED — SAFETY DEVICES FOR AUTOMOBILE PASSENGERS

The people of the United States are immersed daily in a blood bath of automobile-inspired tragedy. Each year 40,000 Americans lose their lives in automobile accidents; 100,000 persons sustain permanent injuries, and another 1,000,000 persons undergo temporary disabilities. A life is lost every 15 minutes day and night, and every 30 seconds someone is injured. According to Campbell,[1] automobiles have killed more Americans during the first 50 years of their existence than were killed collectively during the Revolutionary War, the War of 1812, the Civil War, the various Indian and Mexican wars, the Spanish-American War, World Wars I and II, and the Korean war.

The actual number of deaths and injuries generated by the use of automobiles has multiplied to such an extent that one out of every 10 Americans has an excellent chance to be killed or maimed in highway accidents by the time 1970 rolls around. Indeed, it has been estimated that sooner or later almost every person residing in the United States will be affected by the hazardous course pursued by automobiles.[2]

These grisly figures and estimates—and they cannot be adequately interpreted and measured in blood, tears, or dollars—stress the urgent need for doing something tangible about a perennial national disgrace. Fortunately, the medical profession, which has been among the first to use the automobile in a professional capacity, has been intensely interested in the development of a safe automobile. Proposals have been advanced in various quarters for the purpose of dealing with the mounting carnage, among them the need for incorporating certain basic safety measures in all types of automobiles. Obviously, one of the most important ways of improving safety is to design automobile equipment in terms of human capabilities and limitations.

The principal cause of injury to automobile passengers appears to be uncontrolled motion of the occupants in relation to that of the automobile. Livingstone [3] points out that, in abrupt deceleration, the occupant continues to move forward at approximately the velocity of the automobile in the instant preceding the accident, until he is stopped by impact against the steering wheel, windshield, or dashboard. The rate of deceleration of the occupant under such circumstances may be many times greater than that of the acceleration of gravity.

A number of measures have been brought to the attention of the medical and automotive worlds by Woodward [4] and others regarding the need for protection against the effects of acceleration. The seat belt is a well-known example, and its universal use would undoubtedly save thousands now doomed to die. A securely anchored seat belt holds the occupant firmly in the seat, literally forcing him to "wear the automobile" as a suit of armor. A short time ago a major automobile manufacturer announced that seat belts would soon be available as optional equipment for its automobiles. It is to be hoped that this progressive move will be adopted by all automobile manufacturers as a step in the right direction.

The widespread adoption of other suggested measures to improve the safety of automobile travel would require appreciable changes in the conventional automobile. Some of the medically sponsored changes would include the elimination of all sharp edges and projections in the interior of the automobile; the generous use of padding throughout the automobile; the use of doors that would remain shut during an accident, at the same time being capable of being readily opened during an emergency; the installation of a flexible joint in the steering column that would yield under pressure; the installation of nonrigid dashboards; seats fixed so firmly to the car frame that they can withstand sudden stops; the elevation of the backs of seats in order to support the head and neck; the use of body construction material that would deform or absorb the force of impact; and the installation of "oleo" shock-absorbing bumpers and a "front nose" that would crumble slowly, yet absorb the shock of a crash.

Admittedly, an extensive change in the design of the structure of automobiles would be expensive. Nevertheless, the widespread adoption of safety devices would not cost much, comparatively speaking, when introduced on a mass production basis, and probably not as much as changing the style contours periodically. Automobile manufacturers advertise at considerable cost the thrills and satisfactions of increased acceleration. The time has come to emphasize the more abiding satisfaction of controlled deceleration. This can be done by making automobiles safer, with the occupants properly protected to survive.

1. Campbell, H. E.: Deceleration, Highway Mortality, and the Motorcar, Surgery **36**: 1056 (Dec.) 1954.

2. McFarland, R. A., and Moseley, A. L.: Human Factors in Highway Transport Safety, Boston, Harvard School of Public Health, 1954.

3. Livingstone, R. G.: Automobile Collision Injuries, Surgery **36**: 1059 (Dec.) 1954.

4. Woodward, F. D.: Medical Criticism of Modern Automotive Engineering, J. A. M. A. **138**: 627 (Oct. 30) 1948.

ORGANIZATION SECTION

STATEMENT ON POLIOMYELITIS VACCINE BY DR. WALTER B. MARTIN

Dr. Walter B. Martin, President of the American Medical Association, has publicly assured the cooperation of the medical profession in trying to work out any technical problems related to the use of poliomyelitis vaccine. In a statement released through A. M. A. headquarters Dr. Martin said:

"The rechecking of manufacturing procedures and laboratory data following the outbreak of poliomyelitis in a few vaccinated children has caused unavoidable delay. In the midst of such tension the Eisenhower administration is to be commended for conducting a careful and scientific review of the entire situation before permitting continuance of the program.

"In behalf of myself and the A. M. A. Board of Trustees, I have assured President Eisenhower that the nation's physicians will cooperate in limiting poliomyelitis vaccination to children from five through nine until the vaccine is available in larger supply. Children in this age group who do not receive the vaccine during the current program of the National Foundation for Infantile Paralysis for first and second graders will be vaccinated after its completion.

"The American Medical Association is asking all physicians to administer vaccine only to children in the priority age group of five through nine until further notice. This will assure that the vaccine will be used first for those most susceptible to the disease.

"Physicians are all being asked to keep a record on each child vaccinated. This will include the name and age, the date of vaccination, the site, the manufacturer of the vaccine used and the lot number.

"This voluntary priority vaccination plan follows the recommendation of the National Advisory Committee on Poliomyelitis Vaccination approved by Secretary Oveta Culp Hobby and contained in her report to the President on May 16."

PLANNING GUIDE FOR ESTABLISHING MEDICAL PRACTICE UNITS

A brochure prepared by the Sears-Roebuck Foundation after consultation with the American Medical Association is being made available to members of the A. M. A. on requests placed through their city, county, or state medical societies. It was financed by a grant from the foundation as part of its new health facilities program. The Sears-Roebuck Foundation recently asked the American Medical Association to appoint a medical advisory board to give guidance and advice in connection with other activities of the foundation.

The brochure provides graphically and descriptively a check list for doctors who wish to establish a medical practice unit in a new building, an existing building to be remodeled, or a building to be rented.

The 80-page brochure contains information for physicians setting up practices, expanding practices, or combining with other doctors to develop single medical units. Community leaders who are planning medical units in order to attract physicians to their areas will also find the brochure of interest.

The comparative advantages and disadvantages of building, remodeling, or renting are discussed, and all the factors involved in planning a medical unit are considered. The eight basic elements in the planning of any unit are described: the reception room; the receptionist-control-station business office; the consultation room; the examining and treatment room; the laboratory, including electrocardiographic and basal metabolism apparatus; the x-ray and diagnostic room; the toilet; and the utilities and storage room. Drawings and explanations of each element, along with examples of how these elements can be combined and expanded, are presented. Specific aspects, involving heating, ventilating, air conditioning, plumbing, and wiring are also discussed. Actual management of practice, once the medical unit has been established, is considered in another section. Types of organization, division of income, retirement, sick benefits, death benefits, and settlement of estates are some of the subjects covered.

FEDERAL MEDICAL LEGISLATION

First Session, 84th Congress

Transfer of Hospitals Between Veterans Administration and Defense Department

Congressman Teague (D., Texas) at the request of the Department of Defense, has introduced H. R. 3809, which would authorize the Defense Department to acquire hospitals and related property and equipment from the Veterans Administration without reimbursement. At present, the VA may acquire such property from the Defense Department, but the reverse is not provided for. This bill was referred to the Committee on Veterans' Affairs.

Tax Relief for the Disabled

A series of bills have been introduced to give tax relief for the disabled, or to taxpayers supporting disabled dependents, that would allow such taxpayers an additional $600 exemption for income tax purposes. The bills have varying definitions of disability but do not specifically provide for any finding by a physician. All these bills were referred to the Committee on Ways and Means. The bills were as follows: H. R. 699 by Congressman Rhodes (D., Pa.), H. R. 2580 by Congressman Dingell (D., Mich.), H. R. 3095 and H. R. 3096, by Congressman Dollinger (D., N. Y.), H. R. 3765 and H. R. 3766 by Congressman Fine (D., N. Y.), H. R. 4907 and H. R. 3874 by Congressman Ashley (D., Ohio), H. R. 4278 by Congressman Smith (D., Miss.), H. R. 4491 by Congressman Thompson (D., La.), and H. R. 5184 by Congressman Boggs (D., La.).

Salary Adjustment for Veterans Administration Physicians

Congressman Van Zandt (R., Pa.), in H. R. 3615, would allow full physician's salary for doctors in residency training at a Veterans Administration facility, providing they have had active military service as medical officers since Dec. 7, 1951, and are presently on duty as physicians with the VA. Full-time physicians' salary scale is, of course, higher than that of residents. This measure was referred to the Committee on Veterans' Affairs.

Military Medical and Dental Scholarships

Congressman Bennett (D., Fla.), in H. R. 4645, and Senators Russell (D., Ga.) and Saltonstall (R., Mass.), in S. 1444, have introduced the administration's measures to "facilitate the procurement of doctors of medicine and doctors of dentistry for the Armed Forces by providing grants and scholarships for education in the medical and dental professions." The Defense Department would pay selected students "a monetary allowance at a rate not to exceed $133 per month while under regularly scheduled instruction or training in a school of medicine or a school of dentistry." In addition the government would pay the tuition fees and laboratory expenses of these students. Students accepting such scholarships would be required to serve eight years in the reserve and, if called by the armed services, would serve three years on active duty if they had one year or fractional part thereof of such scholarship benefits. If they had more than one year they could be required to serve four years of active duty. "Two years of active duty, not including time spent in internship, will satisfy active duty requirements of the Universal Military Training and Service Act, as amended." The scholarship board, composed of a chairman and the surgeons general of the armed forces, would counsel on the administration of the act. These bills were referred to the respective committees on armed services.

Prepared by the Washington Office of the American Medical Association.

MEDICAL NEWS

CALIFORNIA

Postgraduate Conferences.—Stanford University School of Medicine, San Francisco, offers postgraduate conferences in internal medicine (registration fee, $75), cardiology (registration fee, $100), and recent advances in general surgery and surgical anatomy (registration fee, $125) June 20-24. Each course is limited to 20 physicians. Checks must accompany applications for registration, which should be mailed to: Office of the Dean, Stanford University School of Medicine, 2398 Sacramento St., San Francisco 15.

Physicians Needed by Health Department.—To encourage recruitment of physicians into state and local health department positions, the state department of public health has made arrangements with separation centers of the Army, Air Force, and Navy in the San Francisco Bay area to provide the department on a current basis with the names of physicians leaving the armed services. Each physician is then contacted by the department and told of opportunities in public health. A statement of "Opportunities in Public Health" has also been distributed to all physicians now with the state and local health departments so that they may assist in the recruitment effort.

Personal.—Dr. Theodore Rothman, Beverly Hills, recently was guest speaker at a meeting of the Central Council of the Union of Turkish Physicians in Istanbul, Turkey. His subject was "Dynamic Pharmacological Psychotherapy."——Capt. Varner J. Johns (MC), formerly associate dean of the School of Medicine, College of Medical Evangelists, Los Angeles, is presently assigned to the professional training branch, office of the Army surgeon general. He came to Washington, D. C., from Fort Sam Houston, Texas, following orientation courses there since last October, when he was ordered to active duty.——Marking his 80th birthday anniversary and 50th year of active practice, Dr. Samuel K. Jamentz, Los Angeles, was honored Dec. 4, 1954, in Pasadena at a dinner attended by more than 100 friends and relatives. Dr. Jamentz, who was born in Armenia in 1874, returned to his native land after graduation from the University of Michigan Medical School, Ann Arbor, in 1904. He later became professor of physical sciences at the Apostolic Institute in Konia, Turkey. After service in the Turkish Army during World War I, he returned to the United States in 1920.——Dr. Peter V. Lee, faculty member of the Stanford University School of Medicine, Stanford University-San Francisco, was recently appointed assistant dean of the University of Southern California School of Medicine, Los Angeles. He will also be a member of the attending staff of the Los Angeles County Hospital in the service of general medicine.

COLORADO

Course on Internal Medicine.—"Fundamental Advances in Internal Medicine" is the title of a course that will be offered by the University of Colorado School of Medicine, Denver, June 13-17, under the sponsorship of the American College of Physicians, with Drs. James J. Waring and Gordon Meiklejohn as co-directors. Fees for members of American College of Physicians, $30; nonmembers, $60. The guest faculty will include: Drs. Richard M. Brickner, New York City; Jerome W. Conn, Ann Arbor, Mich.; Clement A. Finch, Seattle; James A. Greene, Houston, Texas; Hans H. Hecht and Madison H. Thomas, Salt Lake City; Roger S. Mitchell, Burlington, Vt.; Eddy D. Palmer, Washington, D. C.; and Arthur J. Vorwald, Detroit. The course is designed as a survey to present half-day symposia in major subdivisions of internal medicine. Didactic lectures and slides, clinical material, panel discussions, and question periods will be presented. The last hour of each day will be devoted to a radiological conference at which recent advances in diagnosis and therapeutic techniques will be emphasized. This demonstration of roentgenograms will be followed by discussions of the correlation of roentgen and clinical problems. All sessions will be held in the Florence Sabin Amphitheater at the University of Colorado Medical Center, 4200 E. Ninth Ave.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

CONNECTICUT

Three Million Dollar Grant to Yale.—The John A. Hartford Foundation has awarded Yale University, New Haven, a grant of $3,160,000 for research and training in biophysics and the construction of a new research laboratory. The sum will be received in the form of an annual grant of $180,000 for the next 15 years, plus $460,000 for construction of the new biophysics research laboratory on the foundation's property in Valhalla, N. Y. The instructional phase of the new biophysics program will be centered in New Haven, and research activities will be conducted both at Yale and at Valhalla. Ernest C. Pollard, Ph.D., professor of biophysics at Yale, will be chairman of a new department of biophysics. A member of the faculty since 1936, Dr. Pollard has done extensive work in nuclear physics and microwave radar. He helped build Yale's first cyclotron in 1939. For his work in radar, he was awarded a Presidential Certificate of Merit. The new biophysics laboratory at Valhalla, in addition to being the center of a research program, will be used for conference and seminar purposes as well as for summer studies. The first conference, on the Physics of Cellular Processes, was scheduled at Valhalla for Jan. 25-27. Among the research programs to be conducted at the new laboratory will be: (1) studies of the immunizing properties of inactivated virus preparations, involving study of the reaction of animals to challenge doses of viruses and bacteria, and of the serum antibody structure; (2) studies of plant viruses; (3) basic studies in food preservation, which, initially, would deal with bacteria, enzymes, and parts of living cells rather than practical tests on foods.

DISTRICT OF COLUMBIA

Fellowship in Cardiology.—The Metropolitan Heart Guild, Washington, D. C., has established a postdoctorate research fellowship in cardiology in memory of Mrs. Helen H. Millenson, charter member and parliamentarian. The award, carrying a stipend up to $4,000, will be made on an annual competitive basis to a physician who has demonstrated unusual competence for research or possesses specialized training in the field of cardiology. Interested physicians are requested to submit (1) a formal application, stating previous education and training; (2) approval of the contemplated research project for the ensuing year by an institution that will provide necessary facilities if a fellowship award is made; (3) plans for future research work in cardiology; and (4) three confidential letters of reference, submitted under separate cover. All should be addressed to the Metropolitan Heart Guild, % Mrs. Bernard General, Fellowship Chairman, 5056–13th St. N. E., Washington 17, D. C., before Nov. 15. The fellowship award will be announced Jan. 1 of the succeeding year, for the term beginning July 1.

FLORIDA

Dr. Gottlieb Named Director of Neuropsychiatric Clinic.—According to a joint announcement by Wayne University and the Michigan department of mental health, Dr. Jacques S. Gottlieb, who has served as director of the institute of the Jackson Memorial Hospital in Miami, Fla., and chairman of the psychiatry and neurology department at the University of Miami School of Medicine since July, 1953, has been named to the directorship of the nearly completed $3,680,000 Lafayette Clinic, located in Wayne University's medical center in downtown Detroit. He will assume his new duties about July 1. Dr.

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Gottlieb was formerly affiliated with Worcester Hahnemann Hospital in Massachusetts, Montefiore Hospital in New York, and the Iowa State Psychopathic Hospital in Iowa City, where he became assistant director.

IDAHO

State Medical Meeting in Sun Valley.—The 63rd annual meeting of the Idaho State Medical Association will be held at Sun Valley June 19-22 under the presidency of Dr. Alexander Barclay Jr., Coeur d'Alene. The five guest speakers, Drs. James L. Wilson, Ann Arbor, Mich., Paul B. Beeson, New Haven, Conn., Allan C. Barnes, Cleveland, Joel W. Baker, Seattle, and Franklin G. Ebaugh, Denver, will each make four presentations. Social events are planned for each evening during the meeting. The annual barbecue will take place Monday night at the Trail Creek Cabin. On stag night, Tuesday, Donald K. Worden, mayor of Lewiston, will preside. On Wednesday afternoon the guest speakers will participate in the annual round-table session in the Opera House, at which the program chairman, Dr. William R. Jacobs, Lewiston, will preside. Wednesday evening the annual association banquet will be held in the lodge dining room. Each social event is preceded by a social hour.

ILLINOIS

Clinics for Crippled Children.—The University of Illinois division of services for crippled children has scheduled the following clinics, to which any private physician may refer or bring any children for whom he may want examination or consultative services:

June 14, Peoria, Children's Hospital; East St. Louis, Christian Welfare Hospital.

June 15, Chicago Heights, St. James Hospital.

June 22, Springfield (cerebral palsy), Memorial Hospital; Elgin, Sherman Hospital.

June 23, Rockford, St. Anthony Hospital; Bloomington, morning (general), afternoon (cerebral palsy), St. Joseph's Hospital.

June 24, Chicago Heights (rheumatic fever), St. James Hospital.

June 28, Peoria, Children's Hospital; Effingham (rheumatic fever), St. Anthony's Emergency Hospital; Salem, Masonic Temple.

Chicago

Grulee Award to Dr. McCulloch.—The Clifford G. Grulee award was presented to Dr. Hugh McCulloch, chief of staff, La Rabida Jackson Park Sanitarium, at the annual meeting of the American Academy of Pediatrics. Dr. McCulloch served as editor in chief of *Pediatrics*, the official journal of the American Academy of Pediatrics, from the beginning of the publication on Jan. 1, 1948, until he resigned in June, 1954. Dr. Charles D. May, professor of pediatrics, State University of Iowa College of Medicine, University Hospital, Iowa City, is the new editor.

Society News.—At the annual meeting of the Metropolitan Dermatological Society of Chicago the following officers were elected: Dr. Harold W. Thatcher, president; Dr. James J. Barrock, Milwaukee, vice-president; and Dr. Tibor Benedek, secretary-treasurer.——Newly elected officers of the Chicago Society of Physical Medicine and Rehabilitation include: Dr. Joseph L. Koczur, president; Dr. Gusta Davidsohn, vice-president and chairman of the program committee; and Dr. Ralph E. DeForest, secretary-treasurer.——At the annual meeting of the Chicago Dermatological Society, the following physicians were elected: Irene A. Neuhauser, president; John E. Dalton, Indianapolis, vice-president; and Samuel M. Bluefarb, secretary-treasurer.——At the annual meeting of the Chicago Ophthalmological Society, Dr. Daniel Snydacker was elected president; Dr. Kenneth L. Roper, president-elect; Dr. Edward C. Albers, Champaign, Ill., vice-president; Dr. Edward J. Zeiss, Appleton, Wis., councilor; Dr. David E. Shoch, corresponding secretary; and Dr. Frank W. Newell, secretary-treasurer (reelected).——The following were recently named to the board of directors of the Hektoen Institute for Medical Research of the Cook County Hospital: Dr. S. Howard Armstrong Jr., director of medical education, Cook County Hospital; Dr. Arthur R. Colwell, head of department of medicine, Northwestern University Medical School; Dr. Harry F. Dowling, head of the department of medicine, University of Illinois College of Medicine; Dr. Chester C. Guy, chief of surgery, Illinois Central Hospital; and Mr. Charles F. Chaplin, county commissioner.——In recognition of the 60th anniversary of the John Crerar Library at 84 E. Randolph St., the Chicago Heart Association on March 22 presented to the library a copy of the first English edition (1653) of Sir William Harvey's book "Concerning the Motion of the Heart and Blood," and on the same occasion a copy of the first Latin edition (1628) was presented by Mr. Edward L. Ryerson, president of the board of the Chicago Educational Television Association. Dr. Louis N. Katz, president of the Chicago Heart Association, main speaker, was introduced by Dr. George K. Fenn, past-president. A film produced by the Royal Society of Medicine, London, England, delineating Harvey's vital experiments, was shown.

INDIANA

Summer Camp.—A summer camp for physically handicapped children will open July 28 at Bradford Woods, near Martinsville, under the sponsorship of the James Whitcomb Riley Memorial Association. Any ambulatory, physically handicapped child in Indiana who has the approval of his family physician is eligible. Medical services will be supervised by personnel from the Indiana University Medical Center and the James Whitcomb Riley Hospital for Children, Indianapolis.

LOUISIANA

Meeting on Heart Disease.—The Louisiana Heart Association will hold its annual meeting on June 16 in the auditorium of the Louisiana State University School of Medicine, New Orleans. The scientific session at 2 p. m. will be followed by the first annual assembly of the Louisiana Heart Association at 4 p. m. A public forum on heart disease at 8 p. m. will be sponsored by the school and the association.

University News.—The new $3,500,000 addition to the Louisiana State University School of Medicine, New Orleans, was recently dedicated in a ceremony climaxing a day-long observance of the opening. Among the speakers were Troy H. Middleton, B.S., president of the university; Mayor deLesseps S. Morrison; Dr. Maxwell E. Lapham, dean of Tulane University of Louisiana School of Medicine, New Orleans; Dr. Emmett L. Irwin, New Orleans; Dr. Arthur Vidrine, Ville Platte, first dean of the LSU medical school; Dr. Beryl I. Burns, Kansas City, Mo., a former dean; and Dr. F. Warren Raggio, Lake Charles, outgoing president of the Louisiana State University Medical Alumni Association. Dr. William W. Frye, present dean of the LSU medical school, presided. The new wing of the school, adjoined to the school's former front, adds 96,000 square feet to the school's facilities. The addition contains a 650-seat auditorium, a library, a cafeteria, and a radioisotope laboratory, among other facilities.——A laboratory and clinic for the study and treatment of migraine was recently established at the Tulane University of Louisiana School of Medicine, New Orleans, by funds donated by Miss Lallage Feazel and Mr. W. C. Feazel of Monroe and Shreveport. Dr. George E. Burch, Henderson Professor of Medicine and chairman of the department of medicine at Tulane, will direct work in the laboratories, and Dr. John C. S. Paterson and his wife, Dr. Ruth D. Paterson, instructors in medicine, will direct the research work of the laboratory and clinic. The work will be aimed at the "measurement of the phenomena associated with migraine, particularly the disturbance of water metabolism that occurs in the illness." The Feazel Laboratory for the Study of the Cerebral Circulation and Migraine is included in the cardiovascular laboratories in the school of medicine. The clinic to be maintained in connection with the laboratory will be ready to begin service in July.

MAINE

Cardiac, Pediatric, and Orthopedic Clinics.—The state department of health and welfare, division of maternal and child health, will hold a cardiac clinic at the Eastern Maine General Hospital in Bangor, 9 a. m., June 11, and pediatric clinic at 1:30 p. m. Orthopedic clinics have been scheduled as follows: Maine General Hospital, Portland, 9 a. m., June 13; Central Maine General Hospital, Lewiston, 9 a. m., June 17; Community Hospital, Rumford, 1:30 p. m., June 15; and Thayer Hospital, Waterville, 1:30 p. m., June 23.

State Medical Meeting in Rockland.—The 102nd annual session of the Maine Medical Association will convene at The Samoset, Rockland, June 19-21, under the presidency of Dr. William F. Mahaney, Saco. After the opening discussion of defective delinquency in Maine, Dr. Howard B. Sprague, clinical associate in medicine, Harvard Medical School, Boston, will consider "Factors in the Production of Atherosclerosis" under the sponsorship of the Maine Heart Association. At 2 p. m. Dr. Donald S. King, professor of thoracic medicine, Dartmouth Medical School, Hanover, N. H., will present "Modern Concepts in Treatment of Tuberculosis" under the sponsorship of the Maine Tuberculosis Association. "Antibiotics in Pediatrics" will be discussed by Dr. Louis Weinstein, Haynes Department of Infectious Diseases, Massachusetts Memorial Hospitals, Boston (sponsored by the state of Maine Department of Maternal and Child Health). A clambake at 6:30 p. m. will be followed by dancing. On Tuesday morning Dr. John P. L. Madden, director, department of surgery, St. Clare's Hospital, New York City, will talk on gallbladder disease, and Dr. Joseph H. Burchenal, professor of medicine, Sloan-Kettering Division, Cornell University Medical College, New York City, will discuss "Chemotherapy of Blood Dyscrasias" under the sponsorship of the Maine Cancer Society. The Maine Medico-Legal Society, which will present the afternoon program, will have as speaker at its annual business meeting in the morning, former attorney general Alexander LaFleur, who will offer for discussion his views on "A Chief Medical Examiner for Maine," which would involve some radical changes in the medical examiner law. During the afternoon session Dr. A. Warren Stearns, professor of sociology, Tufts College, Medford, Mass., will have as his subject "Murder in Maine." The presidential address will be delivered at the annual banquet, 6:30 p. m., at which the guest speaker will be Herbert Ross Brown, Ph.D., professor of English, Bowdoin College, Brunswick. The woman's auxiliary will hold its meetings simultaneously.

MASSACHUSETTS

Personal.—Dr. Elliott P. Joslin, Boston, honorary president, American Diabetes Association, will give the Banting Memorial Lecture of the British Diabetic Association in Cambridge, England, July 4, at 3:30 p. m. The lecture, entitled "Diabetes for Diabetics," coincides with the opening day of the second Congress of the International Diabetes Federation, which will be held in the same city.

Institute on Cerebral Palsy.—Aided by a $1,500 grant from the United Cerebral Palsy Association, Boston University will present its third annual Institute on the Problems of Children with Cerebral Palsy, June 13-14. A series of lectures, demonstrations, and clinical experiences on current techniques, and information for the education of cerebral palsied children will be offered. Lectures and discussions will be given by leaders in the fields of medicine, education, and guidance, with demonstrations being conducted at the Children's Medical Center, Boston. Other segments of the institute will be held at the Cerebral Palsy Nursery School in Wellesley, Massachusetts Hospital School in Canton, Boston University, and the Joseph P. Kennedy Jr. Memorial Hospital in Brighton. The institute is open to teachers and accredited therapists.

MICHIGAN

Upper Peninsula Convention.—The Upper Peninsula Medical Society will hold its 60th annual convention at the Gateway Hotel, Land O'Lakes, June 17-18, with the Gogebic County Medical Society as host. The convention will open Friday 9 a. m. at Gateway Inn with a panel on cancer, arranged by the Michigan Cancer Coordinating Committee. The moderator, Dr. Darwin M. Nelson, Detroit, will discuss early diagnosis; cancer of the colon will be considered by Dr. James A. Ferguson, Grand Rapids, and cancer of the breast by Dr. Elliott T. Thieme, Ann Arbor. At 10:30 a. m. "Pitfalls in Abdominal Surgery" will be presented by Dr. Frederick A. Coller, Ann Arbor, who will open the afternoon session with "Difficulties Arising in the Surgical Treatment of the Biliary Tract." At 11 a. m. "Present-Day Trends in Use of Hormones in Allergic Disease" will be outlined by Dr. John M. Sheldon, Ann Arbor, whose afternoon presentation will be "Urticaria—Morphological Characteristics and Treatment." Other presentations by guest speakers include:

Infantile Eczema, Harry A. Towsley, Ann Arbor.
Pre- and Postmenopausal Bleeding, Roland S. Cron, Milwaukee.
Errors in Treatment of Commoner Skin Diseases, Harry R. Foerster, Milwaukee.
Prolonged Labor, Tommy N. Evans, Ann Arbor.
Periodic Health Appraisal, John D. Rodger, Bellaire.
Modern Developments in Convulsive Therapy, Z. Stephen Bohn, Grosse Pointe Park.
Low Back Pain, William H. Bickel, Rochester, Minn.
Injection Versus Surgical Treatment of Hemorrhoids, Walter A. Fansler, Minneapolis.
Medical Treatment of Hypertension, Richard M. Schick, Rochester, Minn.

Moderator for the Saturday session will be Dr. Frank J. Hirschboeck, Duluth, Minn. Facilities for golf, tennis, fishing, swimming, archery, skeet, bicycling, and boating are available, and there will be opportunity to take trips to Bond and Agate falls and the copper-mining community of White Pine. A golf tournament, social hours, a banquet, a dance with music by professional entertainers, and a complete program of activities for the ladies are being planned. For reservations and further details write: Dr. Paul R. Lieberthal, 104 S. Suffolk St., Ironwood.

MISSOURI

Grant to Hospital.—Barnes Hospital, St. Louis, has received a grant of $80,628 from the John A. Hartford Foundation of New York. The grant is for the care of indigent patients who have been severely burned. A reduction in the death rate of these patients suffering from traumatic burns has been achieved by the development of a skin bank in the hospital. Expansion of this service will involve additional storage facilities for the bank and equipment. The John A. Hartford Foundation, Inc., was established by the late John A. Hartford, who for many years before his death in 1951 served as president of the Great Atlantic and Pacific Tea Company.

Personal.—Dr. Vincent T. Williams, Kansas City, was honored on Feb. 19 when the world premier of his composition, "Corn and Counterpoint," was given at the Philharmonic pop concert. Dr. Williams is the former editor of *Missouri Medicine* and present editor of the *Kansas City Medical Journal* of the KC Southwest Clinical Society.——Dr. Osamu Hayaishi, assistant professor, department of microbiology, Washington University School of Medicine, St. Louis, since 1952, was recently appointed to lead a new activity in the laboratory of pharmacology and toxicology of the National Institute of Arthritis and Metabolic Diseases, U. S. Public Health Service, where he formerly served for almost two years as a special fellow. He will be concerned with a basic research program on the mechanism of drug action, the intermediary metabolism of drugs and related biochemicals, and biochemical effects of drugs on the body and on bacteria.

NEW HAMPSHIRE

Clinical-Pathological Conference.—Recently the medical staff of the Frisbie Memorial Hospital, Rochester, was host to neighboring hospital staffs at dinner and a clinical-pathological conference presided over by Dr. Allan W. Handy, pathologist to the Frisbie and Exeter hospitals. Special discussors were Dr. Ralph Adams, surgeon-in-chief, Huggins Hospital, Wolfeboro, Dr. William D. Crandall, chief of medicine of the Wentworth Hospital, Dover, and Dr. James T. Heyl, internist and physician of the Exeter Academy, Exeter. The subjects considered were cancer of the body of the pancreas and intractable gastrointestinal bleeding in a form of vascular purpura.

NEW YORK

Course on Electron Microscope.—Cornell University, Ithaca, announces that the summer laboratory course in Techniques and Applications of the Electron Microscope will be given June 13-25 by the laboratory of electron microscopy in the department of engineering physics under the direction of Benjamin M. Siegel, Ph.D. Cecil E. Hall, Ph.D., of M. I. T., Cambridge, Mass., and Robley C. Williams, Ph.D., of the University of California, Berkeley, will be guest lecturers.

Narcotic Violation.—Dr. Claud C. Langley, 272 Clinton Ave., Brooklyn, pleaded guilty to an information charging a violation of the Federal narcotic law in the U. S. district court in Brooklyn. On May 12 he was sentenced to serve a term of two years and was fined $400.

Nutrition Institute in Buffalo.—The 16th annual New York State Nutrition Institute will be held June 14-16 at the Samuel P. Capen Hall, Medical-Dental Building, University of Buffalo, under the sponsorship of the university and the nutrition committee of the Council of Social Agencies of Buffalo and Erie County for the New York State Nutrition Committee. Subjects to be discussed include "Our Changing Food Habits," "The Effect of Under and Over Nutrition in Disease," "What Nutrition Committees Are Doing," "Is Nutrition Education in Tune with the Factors That Influence Our Changing Food Habits?" and "What's New in Food Processing?"

New York City

Personal.—Dr. Harold W. Brown has resigned from the directorship of the Columbia University School of Public Health, effective July 1. He will continue as professor of parasitology, giving instruction in both the medical school and the school of public health and administrative medicine. He will also continue his association with Presbyterian Hospital as consultant in parasitology.

Examinations for Radiation Therapist and Roentgenologist.—The city of New York, department of personnel, Civil Service Commission, 299 Broadway, New York 7, announces examinations for radiation therapist, grade 4, and roentgenologist, grade 4. Applications for full-time employment (roentgenologist) ($5,820 a year) or part-time jobs ($13.825 or $17 a session) will be issued and received, in person or by mail, until 4 p. m. June 23 at the Department of Personnel, 96 Duane St., New York 7. A fee of $4 must accompany application at time of filing. Requests for applications by mail must be accompanied by a 9 in. self-addressed envelope, stamped 6 cents for return. The same rules apply to applications for the position of radiation therapist, grade 4, for which there are eight vacancies. The starting salary is $4,876 a year.

Course in Pediatric Allergy.—New York Medical College Flower and Fifth Avenue Hospitals, division of graduate studies, department of graduate pediatrics, will offer a 30 session postgraduate course in pediatric allergy under the direction of Dr. Bret Ratner, professor of clinical pediatrics and associate professor of immunology, from Nov. 2, 1955, to May 31, 1956. The course, which will be given on Wednesdays from 9 a. m. to 4 p. m., consists of lecture seminars; laboratory and clinical procedures; clinic work; ward rounds and animal experimentation covering basic principles of diagnosis and treatment of allergy in children, and applied immunology. The fee is $300. Applicants must be certified in pediatrics or have the requirements for certification. Enrollment is limited. Apply to the Office of the Dean, New York Medical College, Fifth Avenue at 106th Street, New York 29. A research fellowship in pediatric allergy is available.

Dr. Klumpp Appointed to Rehabilitation Council.—Dr. Theodore G. Klumpp, formerly Secretary of the American Medical Association Council on Pharmacy and Chemistry and now president of Winthrop-Stearns, Inc., has been appointed a member of the National Advisory Council on Vocational Rehabilitation for a four year term by Nelson A. Rockefeller, acting secretary of the Department of Health, Education, and Welfare. The Vocational Rehabilitation Act of 1954 provides for a major expansion of the country's rehabilitation services in a program whose goal is to help restore 200,000 persons a year to useful lives by 1959, the present level being about 60,000 annually. In addition to this appointment, Dr. Klumpp is chairman of the Hoover commission task force on medical services, a director of the World Medical Association and the Commission on Chronic Illness, and from 1936 to 1941 was chief of the drug division, U. S. Food and Drug Administration. In 1951 he was chairman of the Office of Defense Mobilization Task Force on Employment of the Handicapped. He is president of the National Pharmaceutical Council, vice-president of the American Drug Manufacturers' Association, and past-president of the American Pharmaceutical Manufacturers' Association.

OHIO

Conference on Radiation Safety.—A Health Physics Conference, covering the field of radiation safety, will be held June 13-15 at Ohio State University, Columbus. Topics will include radioactive waste disposal, air sampling, dosimetry, health physics instrumentation, legislation, reactor safeguards, and other specialized subjects. Details of the conference may be obtained from Mr. Francis J. Bradley, Superintendent of Radiation Safety, Office of Radiation Safety, Ohio State University, Columbus 10.

Named First Whipple Professor of Pathology.—Dr. James Lowell Orbison, associate professor of pathology at Western Reserve University School of Medicine, Cleveland, has been appointed as the first George Hoyt Whipple Professor of Pathology and head of the department of pathology at the University of Rochester (N. Y.) School of Medicine and Dentistry. The new chair was established through funds provided over a period of 30 years by the Eli Lilly Company for work in the university's pathology laboratory in the study and standardization of secondary anemia liver extracts, under the direction of Dr. Whipple in collaboration with the pharmaceutical firm. Dr. Orbison will succeed Dr. Whipple, who will retire as professor of pathology and head of the department June 30.

OREGON

Society News.—The Eastern Oregon District Medical Society will hold its annual meeting June 17-18 at Enterprise under the presidency of Dr. Bernard R. Sharff of that city. On Friday "Limitations of the Electrocardiogram" by Dr. Marvin Schwartz, Portland, will be sponsored by the Oregon Heart Association. The following panel discussion of rheumatic diseases will be sponsored by the Arthritis Foundation:

Physical Medicine in Rehabilitation of Arthritis, Arthur C. Jones, Portland.

Orthopedics Surgery in the Rheumatic Diseases, George W. Cottrell, Portland.

Steroid Therapy in Rheumatoid Arthritis, Edward E. Rosenbaum, Portland.

Stress and Rheumatoid Arthritis and Etiological Factors in Rheumatoid Arthritis, Robert E. Rinehart, Wheeler.

On Saturday Dr. John H. Fitzgibbon, Portland, will present "Diagnostic Problems of the Gastrointestinal Tract." Dr. Morton J. Goodman, Portland, will talk on practical aspects of antibiotics, and Dr. Herbert V. H. Thatcher, Portland, will discuss "Early Treatment of Hand Injuries." The annual banquet will be held at Wallowa Lake Lodge on Friday. For accommodations write to Dr. George D. Stewart, Joseph.

PENNSYLVANIA

Camp for Preschool Deaf Children.—The Pennsylvania Society for Crippled Children and Adults, in cooperation with the hearing conservation committees of the Medical Society of the State of Pennsylvania and the Pennsylvania Academy of Ophthalmology and Otolaryngology, the Pennsylvania Department of Public Instruction, the University of Pittsburgh, and the Pennsylvania State University, is sponsoring an intensive program for preschool hearing-handicapped children and their families June 12-24 at Laurel Hills State Park near Somerset in western Pennsylvania. The program is directed toward giving diagnostic, educational, and counseling help to the families having deaf children of preschool age. Mothers with their deaf children can attend camp and be given a full-time training period. The fathers are invited to attend camp over weekends to participate in the program. The children must have sufficient hearing loss to interfere with language development, be educable, and not have associated problems such as severe cases of cerebral palsy or visual defects in addition to their hearing loss. Information may be obtained by contacting the Speech and Hearing Clinic, State College, or the Pennsylvania Society for Crippled Children and Adults, 1107 N. Front St., Harrisburg.

WASHINGTON

Meeting on Tuberculosis.—The annual meeting of the Washington Tuberculosis Association will be held at the Benjamin Franklin Hotel, Seattle, June 16-17. The business meetings of the Washington Conference of Tuberculosis Secretaries and the Washington Tuberculosis Association are scheduled for Thursday. At 7 p. m. dinner, dancing, and a cruise aboard the Silver Swan ($3 plus tax) are planned. "Behind the Scenes" by Henry W. Stevens, business manager, National Tuberculosis Association, will be followed by panel discussion of "Medical and Administrative Aspects Involved in Heart, Tuberculosis, and Cancer Case Finding by Means of the Single Miniature Screening Film" Friday morning. "Why Worry About Tuberculosis?" will be presented by Dr. Gardner Middlebrook, director, research and laboratories, National Jewish Hospital, Denver, at luncheon, 12:30 p. m. Friday afternoon will be devoted to a symposium, "The Long Look in Washington," at which Dr. William M. M. Kirby, associate professor of medicine, University of Washington School of Medicine, Seattle, will preside, and in which, case finding will be considered by Dr. Frank S. Miller, Spokane; hospital care, by Dr. Daniel W. Zahn, Seattle; and eradication, by Dr. Cedric Northrop, Seattle. Dr. H. Corwin Hinshaw, clinical professor of medicine and head of the division of chest diseases, Stanford University School of Medicine, San Francisco, dinner speaker (7 p. m.), will present "The Prevention of Illness: A Responsibility of the Private Physician."

WEST VIRGINIA

Society News.—Mr. William H. Lively, Charleston, has been named by the Council as assistant to the executive secretary of the West Virginia State Medical Association. He will assume his new duties July 1. His father, Charles Lively, has served as executive secretary since 1942. Mr. William Lively received his master's degree in journalism from Columbia University, New York City, in June.

Postgraduate Session.—The sixth annual Post Graduate Session of the Barbour-Randolph-Tucker Medical Society will be held at the Tygart Valley Country Club, near Elkins, June 16. The following scientific program will be presented at the afternoon session, beginning at 2 p. m., with Dr. Karl J. Myers, Philippi, serving as moderator:

Headache, Perry S. MacNeal, Philadelphia.
Genital Tract Relaxations, Robert H. Barter, Washington, D. C.
The Physiology of the Thyroid Gland, Maurice Bruger, New York City.
Indications for Surgery in Peptic Ulcer, S. Arthur Localio, New York City.

A question and answer period will follow each address. Kloman Instrument Company, Charleston, and McLain Surgical Supply, Inc., Wheeling, will be hosts at a social hour at 5 p. m. At the banquet, 6:30 p. m., the guest speaker, Dr. Edward J. Van Liere, Morgantown, dean of West Virginia University School of Medicine, Morgantown, will have as his subject "The Present Status and Future Plans for the Medical School at West Virginia University." Honor guests will include Dr. A. Kyle Bush, Philippi, president of the Barbour-Randolph-Tucker Medical Society; Dr. James P. McMullen, Wellsburg, president, West Virginia State Medical Association; and Mr. Charles Lively, Charleston, executive secretary of the state association. A golf tournament is scheduled for the morning of the meeting.

WISCONSIN

University Film Wins Award.—"The Wisconsin Cleft Palate Story," a 16 mm. film produced by the photographic laboratory of the University of Wisconsin extension division, was presented with a Golden Reel award at the annual banquet of the American Film Assembly, National Convention of Non-Theatrical Motion Picture Craftsmen, Distributors and Representatives. The film, selected as the best educational film in the nation, tells how social workers, physicians, plastic surgeons, dental technicians, and speech correctionists combine their efforts to help the 1 in 770 children who have some form of cleft palate or harelip.

Course in Gynecology.—The University of Wisconsin Medical School, Madison, offers a postgraduate course in gynecology (limited to 40 participants) June 21-23. The course will be conducted by Dr. Ralph E. Campbell, professor of obstetrics and gynecology, assisted by the following visiting professors: Drs. John L. Parks, Washington, D. C.; M. Edward Davis and Herbert E. Schmitz, Chicago; Carl S. Harper, Madeline J. Thornton, O. Sidney Orth, and William D. Stovall, Madison. Application for registration should be sent to Dr. Robert C. Parkin, University of Wisconsin Medical School, 418 N. Randall Ave., Madison 6. The registration fee is $5; course fee, $15.

GENERAL

Hearing Society Meets in Chicago.—Ways and means of improving and expanding services for this country's hard of hearing children and adults will be studied during the 36th annual meeting of the American Hearing Society, June 12-14, at the Hotel Morrison, Chicago. Herschel W. Nisonger, president, and Crayton Walker, executive director, will speak at a general meeting Sunday from 8 to 9:30 p. m. Problems of hard of hearing senior citizens will be discussed at a luncheon meeting Monday when papers on "The Older Hard of Hearing Person in the Community" and "The Older Hard of Hearing Person in Homes for the Aged" will be presented.

Meeting of Anesthesiologists.—The Illinois-Indiana-Iowa-Michigan-Minnesota and Wisconsin Anesthesiologists will meet June 12 from 10 a. m. to 12:30 p. m. in the John B. Murphy Memorial Hall of the American College of Surgeons, 40 E. Erie St., Chicago, where the following program will be presented:

Polypharmacy in Anaesthesia, Geoffrey S. W. Organe, London, England.
Paediatric Anaesthesia, Sheila M. Anderson, London, England.
Second Thoughts on Spinal Anaesthesia, Andrew R. Hunter, Manchester, England.
Use and Misuse of Intravenous Needles, Ronald Jarman, London, England.

All physicians, including residents and interns, are cordially invited to attend.

Willard O. Thompson Memorial Fund.—The American College of Physicians announces the establishment of the Willard O. Thompson Memorial Traveling Scholarship Fund in Medicine as a tribute to the memory of the late Dr. Thompson. The aim of the scholarship is to provide an opportunity each year for a qualified and promising young physician to spend one month or more as a visiting fellow at an outstanding institution for postgraduate study under a master clinician. A total of $10,000 is needed to make the fund permanent. Contributions, payable to the "Willard O. Thompson Memorial Traveling Scholarship Fund," may be sent to the American College of Physicians, 4200 Pine St., Philadelphia 4.

U. S. Pharmacopeia XV.—The 15th revision of the U. S. Pharmacopeia will be published July 1. The new standards take effect Dec. 15. There are 838 monographs, of which 242, representing more than 100 new drugs, appear in U. S. P. for the first time. Thus, nearly 30% of the monograph section is entirely new. The groups of drugs showing the greatest increase are the antihistaminics, which increase from 2 to 13 (from 4 to 27 monographs), the antibiotics, which go from 5 to 12, and the diagnostic aids, which go from 9 to 16; the endocrine preparations, including cortisone and its related steroids, increase from 18 to 25. Orders for U. S. P. XV may be placed with the Mack Publishing Company, Easton, Pa., or its agents for filling in the order of their receipt. The price is $10 postpaid for delivery within the United States.

Medical Officers Needed.—According to a recent announcement of the U. S. Civil Service Commission, 82 medical officers are being hired at department of defense establishments in California and Nevada. The commission is accepting applications in all fields of medicine. Most appointments will be made in general medicine and surgery, but specialists in occupational or industrial health; internal medicine and diagnosis; ophthalmology, obstetrics; roentgenology; pediatrics; ear, nose and throat; and orthopedics are also needed. Positions are at government hospitals, supply centers, air stations, shipyards, test centers, and camps and bases. The vacancies are occasioned by the need to replace military personnel with civilian employees. Most of the medical officers will be full-time employees, although a few

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part-time positions will be filled. Information and application forms may be obtained from the commission offices at 630 Sansome St., San Francisco, or from civil service representatives at post offices in California and Nevada.

Meeting on Biological Psychiatry.—The Society of Biological Psychiatry will hold its 10th annual convention at the Palmer House, Chicago, June 11-12, under the presidency of Dr. Harold E. Himwich, Galesburg, Ill., whose reception for members and invited guests will take place at 7 p. m. Sunday. The scientific sessions will open Saturday at 2 p. m. with "Some Aspects of Temporal Lobe Function in Man" by Ward C. Halstead, Ph.D., Chicago. Among the speakers Saturday will be the following Canadians: Dr. Margaret A. Kennard, Vancouver (The Factor of Aggression as Related to the Electroencephalogram); Dr. Hasson Azima, Montreal (Effects of Perceptual Isolation on Mentally Disturbed Individuals); and Drs. Abram Hoffer and Humphry Osmond, Regina and Weyburn, Saskatchewan (Schizophrenia—An Autonomic Disease). An all-day symposium, "Recent Drugs for Treatment of Mental Disease," is planned for Sunday. The presidential address, "Prospects in Psychopharmacology," will open the afternoon session, which will close with a summary of papers on drugs affecting behavior by Dr. Max Rinkel, Boston.

Meeting on Nuclear Medicine.—The Society of Nuclear Medicine will hold its second annual meeting at the Multnomah Hotel, Portland, Ore., June 17-19, under the presidency of Dr. Asa E. Seeds, Vancouver, Wash. The sessions will open at 9 a. m. Friday with "Policy of Radioisotope Laboratory in a General Hospital" by Drs. George D. McGeary and Jeff Minckler, Portland, Ore. At 10:45 a panel seminar on findings of interest in current investigations of the use of radioactive isotopes will have as moderator, Dr. Simeon T. Cantril, Seattle, and as collaborators, Dr. Edwin E. Osgood, Portland, Ore., Dr. Henry Jaffe, Los Angeles, Dr. Leon O. Jacobson, Chicago, and Titus C. Evans, Ph.D., Iowa City. These collaborators will participate also in a panel seminar on practical evaluation of the current status of radioactive isotopes in medical use, with Dr. Howard P. Lewis, Portland, Ore., as moderator, Saturday at 3:30 p. m. A social hour will precede the society banquet, 7 p. m., at which the guest speaker, Dr. John H. Lawrence, Berkeley, Calif., will present "Philosophic and Historical Comments on the Development of Artificial Radioactivity." A family dinner and social evening have been scheduled for Friday.

Grants in Aviation Medicine.—The Link Foundation, Washington, D. C., a trust to advance training and education in aeronautics, has made grants to the Ohio State University, Columbus, and the trustees of Tufts College, Medford, Mass., to establish graduate fellowships in aviation medicine and aviation psychology respectively. Ohio State University has an Aviation Physiology Laboratory, and the college of medicine works closely with North American Aviation, Inc., and the Civil Aeronautics Administration, which has established a medical research laboratory on the campus. The university also administers a Laboratory of Aviation Psychology, directed by Paul M. Fitts, Ph.D., formerly of the Aero Medical Laboratory at the Wright Air Development Center. At Tufts College, which has had an active program in aviation psychology research for many years, Leonard C. Mead, Ph.D., research coordinator and dean of the graduate school, has done considerable aviation research in cooperation with the armed forces, including the U. S. Navy Special Devices Center. Recipient of the fellowship will pursue a full-time graduate program in the department of psychology at Tufts and will conduct thesis research in relation to the aviation research program of the Institute for Applied Experimental Psychology.

American Neurological Association.—The 80th annual meeting of the American Neurological Association is scheduled for June 13-15 at the Palmer House, Chicago, under the presidency of Dr. Percival Bailey, Chicago. After the presidential address at 9 a. m. there will be a symposium on electrical activity of subcortical centers. The Monday afternoon program will open with "Problems in the Diagnosis of Myasthenia Gravis. A 20-Year Report of the Neostigmine Test" by Drs. Henry R. Viets and Robert S. Schwab, Boston, after which "The Effect of Hippocampal Lesions on Recent Memory" will be presented by Drs. Brenda Milner and Wilder G. Penfield, Montreal, Canada. The Monday evening session includes craniovascular studies; studies on human cerebral functions; a paper on amyotrophic lateral sclerosis in the Mariana Islands; a report of 10 cases showing physiological and therapeutic effects of bilateral intermediate midbrain crusotomy for athetodystonia; a discussion of body reflexes acting on the body in injuries to the spinal cord; experimental alterations in pial vascular caliber in the rhesus monkey; and a report on a new blocking agent against the development of LSD-25 psychosis. The Tuesday sessions will open with "Distribution and Relationships of Sympathetic Ganglia in the Splanchnic Region" by Dr. Albert Kuntz, St. Louis, and close with "Handedness and Cerebral Dominance" by Dr. H. Lamar Roberts of Montreal, Canada.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States and its territories and possessions in the weeks ended as indicated:

Area	May 21, 1955		May 22, 1954, Total
	Paralytic Type	Total Cases Reported	
New England States			
Maine	..	..	..
New Hampshire	..	..	..
Vermont	..	..	..
Massachusetts	..	..	1
Rhode Island	..	1	..
Connecticut	..	..	..
Middle Atlantic States			
New York	4	10	2
New Jersey	..	..	..
Pennsylvania	..	10	..
East North Central States			
Ohio	..	5	5
Indiana	..	2	..
Illinois	2	9	2
Michigan	3	5	8
Wisconsin	..	4	1
West North Central States			
Minnesota	..	5	1
Iowa	1	4	1
Missouri	..	1	3
North Dakota	..	..	..
South Dakota	..	..	..
Nebraska	2	4	..
Kansas	..	..	2
South Atlantic States			
Delaware	2	2	..
Maryland	2	2	1
District of Columbia	..	..	1
Virginia	1	5	1
West Virginia	1	3	1
North Carolina	..	2	1
South Carolina	3	4	4
Georgia	5	11	5
Florida	..	7	22
East South Central States			
Kentucky	1	2	1
Tennessee	..	..	3
Alabama	..	3	6
Mississippi	1	3	6
West South Central States			
Arkansas	1	4	3
Louisiana	7	10	9
Oklahoma	..	5	1
Texas	14	37	45
Mountain States			
Montana	3	3	..
Idaho	..	15	1
Wyoming	..	..	..
Colorado	6	12	..
New Mexico	1	1	..
Arizona	..	5	3
Utah	..	..	2
Nevada	..	2	1
Pacific States			
Washington	2	4	4
Oregon	2	4	..
California	21	40	32
Territories and Possessions			
Alaska	..	1	..
Hawaii	2	2	4
Puerto Rico	6	6	..
Total	93	255	183

CANADA

Pediatricians Meet in Quebec.—The combined meeting of the American Pediatric Society, British Paediatric Association, the Society for Pediatric Research, and the Canadian Paediatric Society will be held at the Chateau Frontenac in Quebec, June 15-18.

LATIN AMERICA

Congress of Allergology.—The second International Congress of Allergology will be held in Rio de Janeiro, Brazil, Nov. 6-13, under the chairmanship of Dr. Fred W. Wittich of Minneapolis, president of the International Association of Allergology. Sir Henry H. Dale, London, England; Prof. Pasteur Vallery-Radot, Paris, France; Prof. Bernardo Houssay, Buenos Aires, Argentina; and Dr. Robert Cooke, New York City, have been invited as guest speakers. The official languages will be English, French, Portuguese, and Spanish, and the main topics will be presented in these languages, although scientific communications and discussions may be presented in the native language of the author. North Americans wishing to present papers should send their requests to Dr. Fred W. Wittich, 424 LaSalle Medical Bldg., Minneapolis 2. Information concerning the congress is available from the General Secretary, Dr. Bernard N. Halpern, 197, Boulevard Saint Germain, Paris VII, France, and from the Secretary of the Sociedade Brazileira de Alergia, Dr. Fabiano Alves, Avenida Rio Branco 277, 7 andar, sala 705, Rio de Janeiro, Brazil.

FOREIGN

Meeting of Gynecologists and Obstetricians.—The National Syndicate of Gynecologists and Obstetricians of France has scheduled the second International Syndicate Meeting in Paris, June 27-28, in the Meeting Hall of Medical Societies, 60 Boulevard de Latour-Maubourg. The topic of discussion will be "The Position of the Gynecologist and the Obstetrician in Social Medicine (Social Security, Mutualities, etc.): Methods of Practice and Remuneration." The International Liaison Committee will have its meeting during this conference. All gynecologists and obstetricians may participate in these sessions. For registration and information write to: Dr. J. Courtois, 1, rue Racine, St. Germain en Laye (S. & O.), France.

Life Expectancy in India.—Rajkumari (Princess) Amrit Kaur, who has been India's minister of health since 1937, when India won separate status as a nation, recently announced that in the last five years life expectancy in India has been raised from an average of 27 to 32 years. In that period infant mortality declined from 158 per 1,000 a year to 124 per 1,000, and maternal mortality fell 10%. Great progress was made in the antimalaria campaign, which she described as "one of the triumphs of international cooperation." Top credit for aid to the Indian government in this respect was given to the United Nations Children's Fund, which allocated $667,000 to supply 700 tons of DDT to spray swamps and homes and gave $850,000 worth of equipment for a DDT plant at New Delhi, and to the U. S. Foreign Operations Administration's gifts of DDT for the same purpose.

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AMERICAN ORTHOPEDIC ASSOCIATION, Greenbrier Hotel, White Sulphur Springs, W. Va., June 19-22. Dr. George O. Eaton, 4 East Madison St., Baltimore 2, Secretary.

AMERICAN PEDIATRIC SOCIETY, Chateau Frontenac, Quebec, Canada, June 13-17. Dr. Aims C. McGuinness, Medical Laboratories, University of Pennsylvania, Philadelphia 4, Secretary.

IDAHO STATE MEDICAL ASSOCIATION, Sun Valley, June 19-22. Mr. Armand L. Bird, 364 Sonna Bldg., Boise, Executive Secretary.

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FOREIGN AND INTERNATIONAL

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CONGRESS OF INTERNATIONAL SOCIETY OF SURGERY, Copenhagen, Denmark, July 23-29. Dr. L. Dejardin, 141 rue Belliard, Brussels, Belgium, General Secretary.

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INTERNATIONAL GENERAL MEDICAL CONGRESS, University of Rosario Medical College, Rosario, Argentina, S. A., Nov. 7-12. Dean Jose Imhoff, Santa Fé 3100, Rosario, Argentina, S. A., Chairman.

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PAN AMERICAN CONGRESS OF OPHTHALMOLOGY, Santiago, Chile, S. A., Jan. 9-14, 1956. Dr. Rene Contardo, Huerfanos 930, Of. 74, Santiago, Chile, Secretary General.

PAN AMERICAN CONGRESS ON RHEUMATIC DISEASES, Rio de Janeiro and Sao Paulo, Brazil, S. A., Aug. 14-20. For information write: Dr. Waldemar Bianchi, 126 Avenida Franklin D. Roosevelt, Rio de Janeiro, Brazil, S. A.

PAN AMERICAN MEDICAL SOCIAL CONVENTION, Bogota, Colombia, S. A., Oct. 15-22. Dr. Leopoldo E. Araujo, Avenida de los Presidentes Num. 506, Apartado 2589, La Habana, Cuba, Secretary.

VENEZUELAN CONGRESS OF MEDICAL SCIENCES, Caracas, Venezuela, S. A., Nov. 18-26. Dr. A. L. Briceno Rossi, Apartado 4412, Ofic. del Este, Caracas, Venezuela, S. A., Secretary General.

WORLD CONGRESS OF ANESTHESIOLOGISTS, Scheveningen, Netherlands, Sept. 5-10. For information write: Mr. W. A. Fentener van Vlissingen, Noord-Houdringelaan, 24, Bilthoven, Netherlands.

WORLD CONGRESS ON FERTILITY AND STERILITY, Naples, Italy, May 18-26, 1956. For information address: Prof. G. Tesauro, S. Andrea della Dame, 19, Naples, Italy.

WORLD CONGRESS OF JEWISH PHYSICIANS, Haifa, Tel-Aviv, Jerusalem, Israel, Aug. 10-17. Dr. Z. Avigdori, P.O.B. 1342, Jerusalem, Israel, Chairman.

WORLD CONGRESS OF PHYSICAL THERAPY, New York, New York, U. S. A., June 17-23, 1956. For information address: Miss Mildred Elson, American Physical Therapy Association, 1790 Broadway, New York 19, New York, U. S. A.

WORLD FEDERATION FOR MENTAL HEALTH, Istanbul, Turkey, Aug. 21. For information write: Miss E. M. Thornton, 19 Manchester St., London, W.1, England.

WORLD MEDICAL ASSOCIATION, Vienna, Austria, Sept. 20-26. Dr. Louis H. Bauer, 345 East 46th St., New York 17, N. Y., U. S. A., Secretary General.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Parts I and II in 1955.* June 21-22, Sept. 6-7 (Part I only). Candidates may file applications at any time, but the National Board must receive them at least six weeks before the date of the examination. New candidates should apply by formal registration; registered candidates should notify the board by letter and forward their fees. Exec. Sec., Dr. John B. Hubbard, 133 South 36th St., Philadelphia 4.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* July 15. Final date for filing applications was Jan. 15. *Oral.* New York City, Oct. 23-27. Sec., Dr. Curtiss B. Hickcox, 80 Seymour St., Hartford 15.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Written.* Various centers, June 30. *Oral.* Washington, D. C., Oct. 14-16. Final date for filing application was March 15. Sec., Dr. B. M. Kesten, One Haven Ave., New York 32, N. Y.

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral.* Portland, Ore., Sept. 14-16; Chicago, Nov. 30-Dec. 1. *Subspecialties. Cardiovascular Disease.* Chicago, Nov. 30. The closing date for acceptance of applications for gastroenterology was Feb. 1, and for cardiovascular disease the closing date is June 1. Exec. Sec., Dr. William A. Werrell, 1 West Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* New Haven, November. Oral examinations given in Spring and Fall. Final date for filing application for the Spring examination is October 1; for the Fall examination April 1. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Candidates who participated in the Part I examinations will be notified of their eligibility for the Part II examinations. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Practical Examination.* Chicago, Oct. 9-14. Final date for filing application for 1955 practical examination was July 1, 1954. *Written.* January, 1956. Final date for filing application is July 1. Sec., Dr. Merrill J. King, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Final date for filing application for the Part II examination to be given in January 1956 is Aug 15. Sec., Dr. Harold A. Sofield, 116 South Michigan Ave., Chicago 3.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* Chicago, Oct. 3-7. Final date for filing application is April. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Chicago, Oct. 7-9; and Washington, D. C., Dec. 2-4. Admin. Sec., Mrs. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral and Written.* Philadelphia, Sept. 22-24. Corres. Sec., Miss Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8.

AMERICAN BOARD OF PREVENTIVE MEDICINE: *Certification in Public Health.* Kansas City, Mo., Nov. 10-12. Sec.-Treas., Dr. Ernest L. Stebbins, 615 N. Wolfe St., Baltimore 5.

AMERICAN BOARD OF PROCTOLOGY: *Part II.* Philadelphia, Sept. 17. Sec., Dr. Stuart T. Ross, 131 Fulton Ave., Hempstead, N. Y.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: San Francisco, mid-October; New York City, December. Sec., Dr. David A. Boyd, 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: Chicago, Dec. 4. Final date for filing applications for the fall examination is July 1. Candidates who will complete their training by Dec. 31 will be eligible to appear for this examination. Sec., Dr. B. R. Kirklin, Kahler Hotel Bldg., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Part I.* Centers throughout the United States, in Europe and in the Far East, Oct. 26 and March 28. Closing date for the October examination is July 1 and for the March examination is December 1. *Part II.* Philadelphia, June 13-14; Buffalo, Sept. 26-27; Chicago, Oct. 27-28; New York City, Nov. 14-15; St. Louis, Dec. 12-13; New Orleans, Jan. 16-17; Los Angeles, Feb 13-14; San Francisco, Feb. 16-17; Durham, Mar. 12-13; Boston, May 14-15 and Philadelphia, June 4-5. Sec., Dr. John B. Flick, 255 S. Fifteenth St., Philadelphia 2.

THE BOARD OF THORACIC SURGERY: *Written.* September. Final date for filing applications is July 1. Sec., Dr. Wm. M. Tuttle, 1151 Taylor Ave., Detroit 2.

LATIN AMERICA

Congress of Allergology.—The second International Congress of Allergology will be held in Rio de Janeiro, Brazil, Nov. 6-13, under the chairmanship of Dr. Fred W. Wittich of Minneapolis, president of the International Association of Allergology. Sir Henry H. Dale, London, England; Prof. Pasteur Vallery-Radot, Paris, France; Prof. Bernardo Houssay, Buenos Aires, Argentina; and Dr. Robert Cooke, New York City, have been invited as guest speakers. The official languages will be English, French, Portuguese, and Spanish, and the main topics will be presented in these languages, although scientific communications and discussions may be presented in the native language of the author. North Americans wishing to present papers should send their requests to Dr. Fred W. Wittich, 424 LaSalle Medical Bldg., Minneapolis 2. Information concerning the congress is available from the General Secretary, Dr. Bernard N. Halpern, 197, Boulevard Saint Germain, Paris VII, France, and from the Secretary of the Sociedade Brazileira de Alergia, Dr. Fabiano Alves, Avenida Rio Branco 277, 7 andar, sala 705, Rio de Janeiro, Brazil.

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PAN AMERICAN CONGRESS ON RHEUMATIC DISEASES, Rio de Janeiro and Sao Paulo, Brazil, S. A., Aug. 14-20. For information write: Dr. Waldemar Bianchi, 126 Avenida Franklin D. Roosevelt, Rio de Janeiro, Brazil, S. A.

PAN AMERICAN MEDICAL SOCIAL CONVENTION, Bogota, Colombia, S. A., Oct. 15-22. Dr. Leopoldo E. Araujo, Avenida de los Presidentes Num. 506, Apartado 2589, La Habana, Cuba, Secretary.

VENEZUELAN CONGRESS OF MEDICAL SCIENCES, Caracas, Venezuela, S. A., Nov. 18-26. Dr. A. L. Briceno Rossi, Apartado 4412, Ofic. del Este, Caracas, Venezuela, S. A., Secretary General.

WORLD CONGRESS OF ANESTHESIOLOGISTS, Scheveningen, Netherlands, Sept. 5-10. For information write: Mr. W. A. Fentener van Vlissingen, Noord-Houdringelaan, 24, Bilthoven, Netherlands.

WORLD CONGRESS ON FERTILITY AND STERILITY, Naples, Italy, May 18-26, 1956. For information address: Prof. G. Tesauro, S. Andrea della Dame, 19, Naples, Italy.

WORLD CONGRESS OF JEWISH PHYSICIANS, Haifa, Tel-Aviv, Jerusalem, Israel, Aug. 10-17. Dr. Z. Avigdori, P.O.B. 1342, Jerusalem, Israel, Chairman.

WORLD CONGRESS OF PHYSICAL THERAPY, New York, New York, U. S. A., June 17-23, 1956. For information address: Miss Mildred Elson, American Physical Therapy Association, 1790 Broadway, New York 19, New York, U. S. A.

WORLD FEDERATION FOR MENTAL HEALTH, Istanbul, Turkey, Aug. 21. For information write: Miss E. M. Thornton, 19 Manchester St., London, W.1, England.

WORLD MEDICAL ASSOCIATION, Vienna, Austria, Sept. 20-26. Dr. Louis H. Bauer, 345 East 46th St., New York 17, N. Y., U. S. A., Secretary General.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Parts I and II in 1955.* June 21-22, Sept. 6-7 (Part I only). Candidates may file applications at any time, but the National Board must receive them at least six weeks before the date of the examination. New candidates should apply by formal registration; registered candidates should notify the board by letter and forward their fees. Exec. Sec., Dr. John B. Hubbard, 133 South 36th St., Philadelphia 4.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* July 15. Final date for filing applications was Jan. 15. *Oral.* New York City, Oct. 23-27. Sec., Dr. Curtiss B. Hickcox, 80 Seymour St., Hartford 15.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Written.* Various centers, June 30. *Oral.* Washington, D. C., Oct. 14-16. Final date for filing application was March 15. Sec., Dr. B. M. Kesten, One Haven Ave., New York 32, N. Y.

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral.* Portland, Ore., Sept. 14-16; Chicago, Nov. 30-Dec. 1. *Subspecialties. Cardiovascular Disease.* Chicago, Nov. 30. The closing date for acceptance of applications for gastroenterology was Feb. 1, and for cardiovascular disease the closing date is June 1. Exec. Sec., Dr. William A. Werrell, 1 West Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* New Haven, November. Oral examinations given in Spring and Fall. Final date for filing application for the Spring examination is October 1; for the Fall examination April 1. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Candidates who participated in the Part I examinations will be notified of their eligibility for the Part II examinations. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Practical Examination.* Chicago, Oct. 9-14. Final date for filing application for 1955 practical examination was July 1, 1954. *Written.* January, 1956. Final date for filing application is July 1. Sec., Dr. Merrill J. King, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Final date for filing application for the Part II examination to be given in January 1956 is Aug 15. Sec., Dr. Harold A. Sofield, 116 South Michigan Ave., Chicago 3.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* Chicago, Oct. 3-7. Final date for filing application is April. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Chicago, Oct. 7-9; and Washington, D. C., Dec. 2-4. Admin. Sec., Mrs. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral and Written.* Philadelphia, Sept. 22-24. Corres. Sec., Miss Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8.

AMERICAN BOARD OF PREVENTIVE MEDICINE: *Certification in Public Health.* Kansas City, Mo., Nov. 10-12. Sec.-Treas., Dr. Ernest L. Stebbins, 615 N. Wolfe St., Baltimore 5.

AMERICAN BOARD OF PROCTOLOGY: *Part II.* Philadelphia, Sept. 17. Sec., Dr. Stuart T. Ross, 131 Fulton Ave., Hempstead, N. Y.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: San Francisco, mid-October; New York City, December. Sec., Dr. David A. Boyd, 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: Chicago, Dec. 4. Final date for filing applications for the fall examination is July 1. Candidates who will complete their training by Dec. 31 will be eligible to appear for this examination. Sec., Dr. B. R. Kirklin, Kahler Hotel Bldg., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Part I.* Centers throughout the United States, in Europe and in the Far East, Oct. 26 and March 28. Closing date for the October examination is July 1 and for the March examination is December 1. *Part II.* Philadelphia, June 13-14; Buffalo, Sept. 26-27; Chicago, Oct. 27-28; New York City, Nov. 14-15; St. Louis, Dec. 12-13; New Orleans, Jan. 16-17; Los Angeles, Feb 13-14; San Francisco, Feb. 16-17; Durham, Mar. 12-13; Boston, May 14-15 and Philadelphia, June 4-5. Sec., Dr. John B. Flick, 255 S. Fifteenth St., Philadelphia 2.

THE BOARD OF THORACIC SURGERY: *Written.* September. Final date for filing applications is July 1. Sec., Dr. Wm. M. Tuttle, 1151 Taylor Ave., Detroit 2.

DEATHS

Pomeroy, Lawrence Alson ✙ Shaker Heights, Ohio; born in 1883; Western Reserve University Medical Department, Cleveland, 1908; served on the faculty of his alma mater, where in 1953 he retired as senior clinical instructor in gynecology; past-president of the American Radium Society; past-president and life trustee of the Cleveland Library Association; in 1927 president of the Cleveland Academy of Medicine, which in 1952 presented him with its distinguished service award; in 1947 in recognition of his work on cancer control in Cleveland was presented with a certificate of 10 years' service by the American Cancer Society and in 1951 received a medal for "distinguished service in cancer control"; member of the Radiological Society of North America, Cleveland Radiological Society, Cleveland Surgical Society, Ohio Radiological Society, and the American College of Radiology; fellow of the American College of Surgeons; specialist certified by the American Board of Radiology; for many years director of the tumor clinic at the City Hospital in Cleveland; much of his research in cancer was done at University Hospitals, Cleveland, where he was radium therapist and associate gynecologist; member of the consulting staffs of Lakewood (Ohio) Lutheran Hospital and the Fairview Park, St. Alexis, St. Luke's, and St. John's hospitals in Cleveland; died April 20, aged 71, of cerebral hemorrhage.

Clinton, Fred Severs ✙ Tulsa, Okla.; born in Okmulgee, Indian Territory, April 15, 1874; University Medical College of Kansas City, Mo., 1897; also a graduate in pharmacy; member of the House of Delegates of the American Medical Association in 1906; at one time secretary, treasurer, vice-president, and president of the Indian Territorial Medical Association; in 1927 president of the American Association of Railway Surgeons, of which he was vice-president, 1926-1927; honorary life-president and for many years president of the Oklahoma State Hospital Association, which he organized in 1919; fellow of the American College of Surgeons; during World War I was a member of District Board No. 2 of the Eastern District of Oklahoma and was surgeon of the Student's Army Training Camp, Kendall College Unit, Tulsa; division surgeon for the Midland Valley Railroad; local surgeon for the Sand Springs Railway Company, the Atchison, Topeka and Santa Fe, and the Missouri, Kansas and Texas Railways; author of a chapter on "Indian Territory Medical Association" and the "First Hospitals in Tulsa" in the "Chronicles of Oklahoma"; died in St. John's Hospital April 25, aged 81, of myocardial infarction.

Gumpert, Martin ✙ New York City; born in Berlin, Germany, Nov. 13, 1897; Friedrich-Wilhelms Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1923; clinical associate in physical medicine and rehabilitation, New York Medical College, Flower and Fifth Avenue Hospitals; formerly vice-president of the American Physicians Literary Guild; fellow of the American Geriatric Society; member of the National Committee on Aging, Gerontological Society, and the American Public Health Association; served as a medical orderly with a German Army unit in Turkey during World War I; chief of the geriatric clinic of Jewish Memorial Hospital; on the staff of Goldwater Memorial Hospital; assistant visiting physician for the Metropolitan Hospital and the Bird S. Coler Memorial Hospital and Home; editor of *Lifetime Living Magazine;* medical adviser to *Time Magazine* from 1943 to 1952; author of many books, including "Dunant: Story of the Red Cross," "You Are Younger Than You Think," "Hahnemann: A Medical Rebel," and "The Anatomy of Happiness"; died in the Beekman-Downtown Hospital April 18, aged 57, of heart disease.

McGuire, Louis David ✙ Omaha; born in Wisner, Neb., Sept. 25, 1893; Creighton University School of Medicine, Omaha, 1917; from 1924 to 1929 instructor in surgery at his alma mater, where from 1929 to 1949 he was assistant professor of surgery, in 1949 became associate professor and, since 1951, professor of surgery; a member of the University Lay Board of Regents; specialist certified by the American Board of Surgery; fellow of the International College of Surgeons and the American College of Surgeons; past-president of the Omaha-Douglas County Medical Society and Creighton Alumni Council; served during World War I; associated with the Creighton Memorial St. Joseph's Hospital, St. Catherine's and Children's Memorial hospitals; at one time a fellow in surgery and on the staff of the Mayo Clinic in Rochester, Minn.; on Jan. 23, 1953, received the 1952 American Medical Education Foundation first Award of Merit for outstanding contribution to medical education; died April 20, aged 61.

Markley, Arthur Jackson ✙ San Diego, Calif.; born in Foster, Ky., Jan. 11, 1874; Miami Medical College, Cincinnati, 1903; since 1945 professor emeritus of dermatology and syphilology at the University of Colorado School of Medicine in Denver; specialist certified by the American Board of Dermatology and Syphilology; an associate member of the American Medical Association; member of the American Dermatological Association; president of the Colorado State Medical Society, 1936-1937, and formerly a member of the board of trustees; in 1929 president, and at one time a member of the board of trustees of the Denver Medical Society; in the late 1930's was one of the founders and a member of the first board of trustees of Colorado Hospital Service (Blue Cross); in 1911 founded and became the first editor of the *Denver Medical Bulletin;* died March 20, aged 81, of chronic myocarditis.

Clapp, Clyde Alvin ✙ Baltimore; born in Chatham, Ohio, May 29, 1880; Baltimore Medical College, 1902; professor of ophthalmology emeritus at the University of Maryland School of Medicine and College of Physicians and Surgeons; associate professor emeritus of ophthalmology at Johns Hopkins University School of Medicine; member of the American Academy of Ophthalmology and Otolaryngology, American Ophthalmological Society, and the Association for Research in Ophthalmology; fellow of the American College of Surgeons; vice-president, member of the board of governors, and member of the staff of the Baltimore Eye, Ear and Throat Hospital; ophthalmologist at St. Vincent's Infants Asylum; specialist certified by the American Board of Ophthalmology; author of "Cataract: Its Etiology and Treatment"; died April 9, aged 74, of carcinoma of the stomach.

Lenhart, Carl Henri ✙ Cleveland; born in 1880; Western Reserve University Medical Department, Cleveland, 1904; professor emeritus of surgery at his alma mater, where on Dec. 6, 1932, he was appointed professor and head of the department of surgery, and in 1933, when the Oliver H. Payne chair of surgery was established, was appointed the first to occupy the new professorship; member of the founders group of the American Board of Surgery; member of the American Surgical Association; fellow of the American College of Surgeons; served several terms as president of the Cleveland Medical Library Association, of which he was for 18 years directing librarian; retired chief of surgery, University Hospitals of Cleveland, and director, surgical division, City Hospital; died in the University Hospital April 8, aged 74, of arteriosclerotic heart disease.

Doyle, Thomas Lawrence ✙ Philadelphia; born in Tremont, Pa., July 1, 1894; Hahnemann Medical College and Hospital of Philadelphia, 1916; professor of plastic and reconstructive surgery at his alma mater; specialist certified by the American Board of Plastic Surgery; fellow of the International College of Surgeons and the American College of Surgeons; during World War I served as a captain in the medical corps of the U. S. Army and attached to British Expeditionary Forces; decorated with the Military Cross by King George V for great gallantry and devotion to duty; received the Purple Heart; plastic and reconstructive surgeon at the Hahnemann Hospital; medical director of the Insurance Company of North America; died in the Hahnemann Hospital April 7, aged 60.

✙ Indicates Member of the American Medical Association.

Thomas, Harry Vernon ✠ Clarksburg, W. Va.; born in Alexandria, Ind., Dec. 19, 1895; Johns Hopkins University School of Medicine, Baltimore, 1925; certified by the National Board of Medical Examiners; specialist certified by the American Board of Ophthalmology; member of the Southeastern Surgical Congress, American Academy of Ophthalmology and Otolaryngology, and Association for Research in Ophthalmology; fellow of the American College of Surgeons; past-president of the Harrison County Medical Society; served during World War I; held the rank of lieutenant (jg) in the medical corps of the Navy from 1925 to 1927; on the staffs of the St. Mary's, Union Protestant, and Veterans Administration hospitals; died April 21, aged 59, of heart disease.

Madden, John Francis ✠ St. Paul; born in Hillsboro, Wis., Sept. 22, 1901; University of Minnesota Medical School, Minneapolis, 1926; clinical associate professor of medicine (dermatology) at the University of Minnesota Medical School, Minneapolis, and the University of Minnesota Graduate School, Minneapolis-Rochester; specialist certified by the American Board of Dermatology and Syphilology; member of the American Dermatological Association and the American Academy of Dermatology and Syphilology; associated with the Gillette State Hospital for Crippled Children, the Ancker, Charles T. Miller, St. Joseph's, St. Luke's, and Bethesda hospitals, and the University of Minnesota Hospitals in Minneapolis; died March 9, aged 53, of coronary occlusion.

Durbin, Edgar ✠ Denver; born in Denver May 14, 1903; Harvard Medical School, Boston, 1929; formerly on the faculty of the University of Colorado School of Medicine; certified by the National Board of Medical Examiners; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; past-president of the Denver County Medical Society and the Colorado Heart Association; served during World War II; on the staffs of the St. Luke's, Childrens, Presbyterian, Mercy, Denver General, Colorado General, and St. Joseph's hospitals; died March 21, aged 51, of coronary thrombosis.

Bower, Richard Leslie ✠ Carmel, Calif.; born in Chicago Feb. 26, 1892; Northwestern University Medical School, Chicago, 1920; specialist certified by the American Board of Ophthalmology and the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; formerly practiced in Kansas City, Mo., where he was on the staffs of the Research, St. Luke's, and Trinity Lutheran hospitals; on the staffs of the Peninsula Community Hospital in Carmel and the Monterey (Calif.) Hospital; died March 26, aged 63, of cerebral embolism.

Raleigh, Gordon Woodrow ✠ Evanston, Ill.; born in Salt Lake City May 18, 1913; Northwestern University Medical School, Chicago, 1942; assistant professor of medicine at his alma mater, where he was chairman of the graduate education committee; specialist certified by the American Board of Internal Medicine; an associate member of the American College of Physicians; member of the American Diabetes Association, American Heart Association, and Alpha Omega Alpha; served during World War II; on the staff of the Evanston Hospital, where he died April 13, aged 41, of acute myocardial insufficiency.

Chatigny, Joseph Victor ✠ Taunton, Mass.; College of Physicians and Surgeons, Boston, 1916; member of the New England Obstetrical and Gynecological Society and the New England Society of Psychiatry; president of the Bristol North District Medical Society from 1947 to 1949; served during World War I; examining physician of Selective Service Board 148 in World War II; associate medical examiner and school physician; director of the Mechanics Cooperative Bank for eight years; associated with the Foxboro (Mass.) State Hospital, Taunton State, and Morton hospitals; died March 24, aged 64.

Halsey, Levi Wright ✠ Montclair, N. J.; College of Physicians and Surgeons, Baltimore, 1883; an associate member of the American Medical Association and in 1923 member of the House of Delegates; past president of the Suffolk County (N. Y.) Medical Society; at one time practiced in Bridge Hampton, N. Y., where he was coroner of Suffolk County; formerly member of the board of health; president of the staff, 1923-1924, and for many years associated with the Mountainside Hospital, where he died March 10, aged 94, of carcinoma of the prostate and arteriosclerotic heart disease.

Honor, William Hilliard ✠ Wyandotte, Mich.; born Jan. 17, 1879; Detroit College of Medicine, 1903; member of the American Association for the Surgery of Trauma; fellow of the International College of Surgeons and the American College of Surgeons; member and past-president of the Detroit Academy of Surgeons; served overseas during World War I and was awarded the American Distinguished Service medal and the rosette of the French Legion of Honor; for many years chief of surgery at Wyandotte General Hospital, where he died March 7, aged 76, of coronary occlusion.

Carrigan, Thomas Alva ✠ Denton, Texas; born in Cleburne Dec. 7, 1913; University of Texas School of Medicine, Galveston, 1938; past president of the Brown-Comanche-Mills-San Saba Counties Medical Society; while in the medical corps of the U. S. Army during World War II, served in Africa and Italy with the Forty-Seventh Armored Medical Battalion of the First Armored Division; received a citation for heroic service in December, 1944, and was awarded the Bronze Star in April. 1945; died in the Flow Memorial Hospital Jan. 29, aged 41, of cerebral hemorrhage.

Hocker, Ulysses Washington ✠ Lewis, Del.; born in 1870; Long Island College Hospital, Brooklyn, 1891; past-president of the Medical Society of Delaware; for two terms mayor; for many years president of the board of education of Lewes; member of the advisory board of the Beebe Hospital; served 13 years as chairman of the board of directors of the Lewes Branch of the Sussex Trust Company, from which he resigned in November, 1949; a charter-member and in 1930 president of the Rotary Club of Lewes; died in Seaford Feb. 6, aged 85, of cerebral arteriosclerosis.

Arimizu, Richard Hatsuhiko, Hilo, Hawaii; Harvard Medical School, Boston, 1932; certified by the National Board of Medical Examiners; died recently, aged 49, of bronchopneumonia.

Austraw, Harrison Henry, Houston, Texas; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1934; member of the American Academy of General Practice; served during World War II; died April 6, aged 49, of coronary thrombosis.

Bauman, Charles Martin ✠ St. Louis; St. Louis University School of Medicine, 1911; died in St. John's Hospital March 28, aged 67, of coronary arteriosclerotic heart disease.

Bennett, Charles Lafayette ✠ Los Angeles; Chicago Homeopathic Medical College, 1890; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1897; an associate member of the American Medical Association; on the staff of the California Hospital; died in the Sawyer Sanatorium in Marion, Ohio, April 6, aged 84, of heart failure.

Black, Walter B. ✠ Austin, Texas; University of the South Medical Department, Sewanee, Tenn., 1901; on the staff of the Brackenridge Hospital; died March 31, aged 76, of coronary heart disease.

Bone, Pinckney Seymour ✠ Lancaster, Ohio; Ohio Medical University, Columbus, 1903; died March 8, aged 81, of carcinoma of the prostate.

Brandstein, Joseph S., New York City; Columbia University College of Physicians and Surgeons, New York, 1921; associated for 25 years with the Department of Hospitals; on the staffs of the Lebanon and Bronx hospitals; died in the Montefiore Hospital April 7, aged 57, of coronary occlusion.

Brinker, Samuel Peter, Uniontown, Pa.; College of Physicians and Surgeons, Baltimore, 1905; died in Uniontown Hospital March 17, aged 78.

Brooks, William Wilkerson ✠ Borger, Texas; University of Tennessee College of Medicine, Memphis, 1920; member of the Industrial Medical Association; on the staff of the North Plains Hospital; director of the First National Bank of Borger; died March 24, aged 59, of coronary occlusion.

Brown, Louis Gordon ✦ Colorado Springs, Colo.; Denver College of Medicine, 1902; member of the American Roentgen Ray Society and the Radiological Society of North America; an associate member of the American Medical Association; died Feb. 25, aged 85, of sarcoma.

Brunson, Eugene Taylor ✦ Ganges, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1906; died in San Pedro, Calif., March 30, aged 75, of rupture of the abdominal aorta.

Burkhard, Edwin Dalp, Aurora, Colo.; University of Pennsylvania Department of Medicine, Philadelphia, 1895; died Feb. 25, aged 84, of arteriosclerosis.

Burton, George Marshall ✦ Clinton, N. J.; University College of Medicine, Richmond, 1901; member of the West Virginia State Medical Association; formerly practiced in Weston, W. Va., where he was on the staff of the City Hospital; died April 16, aged 80, of dilatation of the heart.

Bynum, Joseph Medicus, Booneville, Miss.; Vanderbilt University School of Medicine, Nashville, Tenn., 1901; served as city health officer; died Jan. 12, aged 78, of cerebral thrombosis.

Carter, James Thomas ✦ Spartanburg, S. C.; Medical College of the State of South Carolina, Charleston, 1904; past-president of the Spartanburg County Medical Society; died March 24, aged 76.

Courvoisier, Earl Alfred, St. Petersburg, Fla.; Chicago Medical School, 1921; member of the Association for Research in Ophthalmology; died in Mound Park Hospital April 4, aged 61, of acute tracheobronchitis.

Cunnane, Thomas Edward, Ventura, Calif.; Cooper Medical College, San Francisco, 1893; served on the state lunacy commission, the local school board, and the library commission; member of the city council; died April 20, aged 88, of cerebrovascular thrombosis and generalized arteriosclerosis.

Daley, Mark Joseph ✦ Yonkers, N. Y.; McGill University Faculty of Medicine, Montreal, Canada, 1921; member of the Association for Research in Nervous and Mental Disease; consultant on neuropsychiatry at North Hudson Hospital in Weehawken; on the staffs of the Yonkers General, St. John's Riverside, and St. Joseph's hospitals, where he died April 11, aged 61, of ruptured aortic abdominal aneurysm.

Davis, Thomas Miller ✦ St. Louis; Washington University School of Medicine, St. Louis, 1911; member of the American Society of Anesthesiologists; on the staffs of De Paul Hospital and St. Luke's Hospital, where he died April 5, aged 67, of cardiovascular renal disease.

Denman, Robert D., Helmer, Ind.; Medical College of Indiana, Indianapolis, 1905; member of the Indiana State Medical Association; at one time principal and superintendent of schools at Mercer, Ohio; died in Sacred Heart Hospital, Garrett, March 27, aged 81, of injuries received in an automobile accident.

Denney, Benjamin F., Britt, Iowa; Chicago College of Medicine and Surgery, 1909; served on the board of health and school board; on the staff of the Hancock County Memorial Hospital, where he died March 17, aged 71, of cerebral vascular accident.

Donovan, John Elmer ✦ Erie, Pa.; Boston University School of Medicine, 1931; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; director of the school board; member of the staffs of the Erie County Tuberculosis Hospital, St. Vincent's Hospital, and the Hamot Hospital; died April 6, aged 51, of coronary disease.

Fiedelman, Harry Lewis ✦ Brooklyn, N. Y.; New York Homeopathic Medical College and Flower Hospital, New York City, 1930; associated with the Kings County Hospital; died March 17, aged 49.

Fishbaugh, Guy Wood, Minford, Ohio; Ohio State University College of Medicine, Columbus, 1914; health commissioner for Scioto County from 1932 to 1947; died March 6, aged 66, of a heart attack.

Fisher, Emerson Webster, Arnold, Neb.; Rush Medical College, Chicago, 1892; at one time practiced in Portage, Ohio, where he was village mayor; served during World War I; died March 17, aged 84, of bilateral lobar pneumonia.

Friedman, Gerald Herman ✦ Denver; Marquette University School of Medicine, Milwaukee, 1927; fellow of the International College of Surgeons; clinical instructor in surgery at the University of Colorado School of Medicine; served during World War II; member of the staff of the General Rose Memorial Hospital, where he died March 19, aged 55, of carcinoma of the pancreas.

Gibson, Albert Mathew, Lower Peach Tree, Ala.; Medical College of Alabama, Mobile, 1885; Jefferson Medical College, Philadelphia, 1903; died March 31, aged 88, of cardiovascular disease.

Glass, Thomas William ✦ Weslaco, Texas; University of Texas School of Medicine, Galveston, 1916; past-president of the Hidalgo-Starr Counties Medical Society; served overseas during World War I; at one time health officer; for many years in charge of football teams of Weslaco High School; died in Mercedes Feb. 26, aged 69, of hypertensive cardiovascular disease.

Hansen, Hans, Logan, Iowa; John A. Creighton Medical College, Omaha, 1905; specialist certified by the American Board of Psychiatry and Neurology; past-president of the Harrison County Medical Society; member of the American Psychiatric Association; fellow of the American College of Physicians; formerly manager of the Veterans Administration Hospital in St. Cloud, Minn., and Canandaigua, N. Y.; died in Jennie Edmundson Hospital in Council Bluffs Feb. 22, aged 76, of pneumonia and arteriosclerotic heart disease.

Hartley, John Edwin ✦ Denver; St. Louis University School of Medicine, 1923; on the staffs of the St. Joseph's Hospital and the Mercy Hospital, where he died March 2, aged 55, of thrombosis of the spleen.

Hendricks, John DeWitt ✦ Indianapolis; Indiana Medical College, School of Medicine of Purdue University, Indianapolis, 1906; on the staff of the Methodist Hospital, where he died March 21, aged 80.

Huston, Abraham Lincoln, Mariemont, Ohio; Illinois Medical College, Chicago, 1896; died March 29, aged 87, of cerebral hemorrhage.

Hutchinson, William Orrin ✦ Richmond, Vt.; Hahnemann Medical College and Hospital of Philadelphia, 1905; served during World War I; served on the staffs of the Fanny Allen Hospital in Winooski, and the Bishop DeGoesbriand and Mary Fletcher hospitals in Burlington; died in Burlington March 26, aged 74.

Hutto, William S., Damascus, Ark. (licensed in Arkansas in 1903); died in the Conway (Ark.) Memorial Hospital March 26, aged 79, of coronary thrombosis.

Hutton, John Evans ✦ New York City; Syracuse University College of Medicine, 1921; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; associated with the Woman's and Gouverneur hospitals; on the staff of the Roosevelt Hospital, where he died April 8, aged 57, of cerebral hemorrhage.

Kirk, Obe Atha ✦ Linden, Tenn.; University of Tennessee College of Medicine, Memphis, 1912; president of the Hickman and Perry Counties Medical Society; county health officer; died March 30, aged 70, of coronary occlusion.

Krystaniak, Matthew F., Buffalo; University of Buffalo School of Medicine, 1915; member of the Medical Society of the State of New York; on the staff of Sisters of Charity Hospital; died March 6, aged 62, of adenocarcinoma of the rectum.

Lamson, Margaret Eunice, San Francisco; Stanford University School of Medicine, San Francisco, 1924; on the staff of the French Hospital; died in the Community Hospital, San Mateo, June 10, aged 65, of cerebral embolus and myocardial infarction.

Landau, Irving Isaac ✦ Billerica, Mass.; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1934; died Feb. 27, aged 49.

McCarthy, David Henry ✦ Springfield, Ill.; Chicago College of Medicine and Surgery, 1912; died in St. John's Hospital March 27, aged 68, of arteriosclerotic heart disease.

McElroy, Homer Adaway, Columbia, S. C.; University of Georgia Medical Department, Augusta, 1914; since Sept. 20, 1916, associated with the South Carolina State Hospital; died March 24, aged 70, of coronary occlusion.

McLaughlin, Charles Molten, Freeport, Pa.; Jefferson Medical College of Philadelphia, 1904; member of the Medical Society of the State of Pennsylvania; one of the original members of the staff of the Allegheny Valley Hospital, Tarentum, where he died Feb. 9, aged 76, as the result of an automobile accident.

Maclay, Joseph Alan ✦ Paterson, N. J.; Jefferson Medical College of Philadelphia, 1902; served during World War I; consultant at the Paterson General Hospital, where he died March 27, aged 76, of cerebral hemorrhage, cerebral arteriosclerosis, and carcinoma of the prostate.

Melnik, Morris ✦ Los Angeles; University of Michigan Medical School, Ann Arbor, 1932; interned at the Cedars of Lebanon Hospital, where he served a residency; died in the Peter Bent Brigham Hospital, Boston, Jan. 24, aged 46, of respiratory collapse following an operation.

Mercer, Nathaniel Allan ✦ Columbia, Ky.; University of Louisville (Ky.) School of Medicine, 1931; for many years county health officer; died in the Norton Memorial Infirmary, Louisville, March 28, aged 50, of coronary artery disease.

Merritt, Clifton Ernest ✦ Manton, Mich.; Indiana University School of Medicine, Indianapolis, 1930; chief of district number 1 health department; past-president of the Michigan Health Officers Association; died in the Mercy Hospital, Cadillac, March 22, aged 52.

Mick, Edwin Carl ✦ East Orange, N. J.; Queen's University Faculty of Medicine, Kingston, Ontario, Canada, 1916; served in the Canadian Army in France and Belgium during World War I; on the staffs of the Orange Memorial and St. Mary's hospitals in Orange; died in West Orange March 28, aged 68, of coronary occlusion.

Montgomery, James, Van, Texas; Memphis (Tenn.) Hospital Medical College, 1897; died March 26, aged 79, of urinary tract infection and hypertrophy of the prostate.

Mouser, Ray Henry ✦ Paulding, Ohio; Ohio State University College of Medicine, Columbus, 1917; served overseas during World War I; president of the National Bank of Paulding; associated with the Paulding Memorial Hospital, where he died March 15, aged 59, of cardiac asthma and uremia.

Moye, Leon G., Adrian, Ga.; Maryland Medical College, Baltimore, 1904; for many years mayor; died in the Emanuel County Hospital, Swainsboro, March 23, aged 74, of coronary thrombosis.

Reese, George Grant, Yardley, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1922; fellow of the American College of Surgeons; interned at the Wilkes-Barre City (Pa.) Hospital; died in the Mercer Hospital, Trenton, N. J., March 26, aged 56, of cancer.

Richmond, F. E. ✦ Stockton, Kan.; Central Medical College of St. Joseph, Mo., 1897; Kansas City (Mo.) Medical College, 1902; city and county health officer; associated with the Hadley Memorial and St. Anthony's hospitals in Hays; died Feb. 22, aged 82, of coronary occlusion.

Rooney, James Francis ✦ Plainville, Conn.; Baltimore Medical College, 1903; served during World War I; formerly practiced in Hartford, where he was school medical examiner, member of the board of health and physician for the county jail; consultant in urology at St. Francis Hospital, Hartford, where he was president in 1941 of the medical and surgical staff and where he died March 27, aged 75, of carcinoma of the lung with metastases to right shoulder.

Sachs, Gerhart Harry, New York City; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1921; died in the Medical Arts Center Hospital Jan. 30, aged 57, of aplastic anemia.

Scheifly, John Edward ✦ Kingston, Pa.; Jefferson Medical College of Philadelphia, 1897; past-president of the Luzerne County Medical Society and the Luzerne County Ophthalmological Society; at one time practiced in Edwardsville, where he was president of the board of health for 10 years and president of the school board for 2 years; a trustee of Nesbitt Memorial Hospital; a director of the Kingston National Bank, of which he was president for four years; died April 17, aged 81, of arteriosclerosis and hypoplastic anemia.

Schintzius, William Charles ✦ Boonville, N. Y.; University of Buffalo School of Medicine, 1926; past-president of the Oneida County Medical Society; served overseas during World War II; died March 27, aged 54, of injuries received when the automobile in which he was driving was struck by a truck.

Scudder, John Arrell ✦ Edwardsport, Ind.; Indiana Medical College, School of Medicine of Purdue University, Indianapolis, 1906; member of the staff of Good Samaritan Hospital in Vincennes, where he was a member of the board of directors of the Hillcrest Tuberculosis Hospital; died in the Robert W. Long Hospital, Indianapolis, March 30, aged 73, of postoperative pneumonia.

Shattuck, George L. ✦ Providence, R. I.; University of Vermont College of Medicine, Burlington, 1892; served on the staffs of the Butler, Rhode Island, Charles V. Chapin, and Roger Williams hospitals; died March 20, aged 87, of cerebral thrombosis and coronary occlusion.

Smith, Harold Francis ✦ Iowa City, Iowa; State University of Iowa College of Medicine, Iowa City, 1921; served during World War II; on the staff of the Mercy Hospital, where he died March 25, aged 57, of carcinoma of the lung.

Smith, John David, Jay, N. Y.; University of Vermont College of Medicine, Burlington, 1906; served as town clerk and health officer of Jay; for many years secretary of the Essex County Agricultural Society; supervisor of the school board; on the staff of Champlain Valley Hospital in Plattsburg, where he died March 26, aged 75, of arteriosclerotic heart disease and a virus infection.

Smith, Risdon Ernest, Minden, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1907; member of the Louisiana State Medical Society and the Southeastern Surgical Congress; fellow of the American College of Surgeons; on the staff of the Minden Sanitarium; died March 25, aged 70, of pulmonary emphysema.

Thomas, Gordon Augustus ✦ Lafayette, Ind.; Indiana University School of Medicine, Indianapolis, 1918; died in St. Elizabeth's Hospital March 9, aged 63, of coronary thrombosis.

Treadway, Lucien, Canandaigua, N. Y.; Kentucky School of Medicine, Louisville, 1903; died in the Veterans Administration Hospital Jan. 1, aged 78, of bronchopneumonia.

Turner, John Hazelett III ✦ Glen Olden, Pa.; Medico-Chirurgical College of Philadelphia, 1914; served during World War I; since 1936 coroner's physician of Delaware County; on the staff of Chester (Pa.) Hospital; died March 8, aged 66, of coronary occlusion.

Wallace, William Davies ✦ New Castle, Pa.; Jefferson Medical College of Philadelphia, 1920; on the staff of the Jameson Memorial Hospital; died March 6, aged 60, of terminal pneumonia and multiple myeloma.

White, Emory Owen, Hamburg, Ark. (licensed in Arkansas in 1907); member of the Arkansas Medical Society; died in the Crossett (Ark.) Health Center March 31, aged 72, of coronary occlusion.

Wiener, Samuel H. ✦ Chicago; Chicago College of Medicine and Surgery, 1913; on the staff of the Mother Cabrini Memorial Hospital; died May 7, aged 66, of ruptured abdominal aortic aneurysm and arteriosclerosis.

Zellmer, Carl Edward ✦ Antigo, Wis.; University of Pennsylvania School of Medicine, Philadelphia, 1919; member of the American Academy of General Practice; died in Mendota, Ill., March 14, aged 61, of injuries received in an automobile accident.

FOREIGN LETTERS

BRAZIL

Special Service of Public Health.—Dr. E. P. Campbell, until recently the American director of the Special Service of Public Health, a joint United States-Brazil organization, left for Washington, D. C., terminating his connection with the service, to which he had devoted almost 10 years. The Special Service is an outcome of the effort of the United Nations to win World War II. The execution of a broad program of health and sanitation in the South American republics with the financial help of the United States was one of the recommendations of the Third Meeting of the Ministers of Foreign Affairs held at Rio de Janeiro in January, 1942. The need for Brazil to increase the exploitation of the raw materials indispensable to the war effort pointed to the organization of a special service of public health for the states of Pará and Amazonas, where rubber trees are native. Later, other projects were included in the program. About 20 million dollars has already been spent for the benefit of the 5 million Brazilians inhabiting the areas where the Special Service is operating. The results are limited by the number of Brazilian and American technicians who can be trained and by the financial resources appropriated to the organization. The training of a multiplicity of highly specialized technicians is the key to the success of the venture.

Small hospitals have been installed and are being supported in whole or in part by the Special Service in several states. The service also founded and is running 40 county health units on a full-time basis in four states. In the last few years, about 4 million visits were registered at the clinics of the health units and about 500,000 patients received medical care, 2,800,000 prescriptions were filled, 1,200,000 dressings were made, and 1,400,000 injections were given. Other important activities of the service are the planning and construction of water supply and sewage disposal units in scores of towns in various states. Before leaving, Dr. Campbell signed, in the name of the American government, a contract with the government of Brazil to prolong for five years the technical and financial cooperation of the United States in the administration of the service. Until June, 1960, the United States will contribute the total sum of $300,000, to be supplemented by $2,500,000 from the Brazilian government. This will permit the completion of several projects and increase the number of trained technicians.

Mitral Disease.—At a meeting of the Associacão Paulista de Medicina, Dr. Santos Filho and his co-workers analyzed 87 cases of pure or predominantly stenosal lesions of the mitral valve in the first 100 patients with mitral disease operated on at the São Paulo State University Hospital. Starting from a classification of the different types of lesions caused by acute polyarticular rheumatism of the mitral valve (orificial, valvular, commissural, cordal, and rigid dysfunctional), the authors tried to correlate the type of lesion found by the surgeon with the clinical results obtained. They found that fibrotic and calcified valves are more frequent in men with pure as well as with mixed lesions. The authors decided to verify in each case of pure mitral stenosis whether the surgeon might have made a good or bad opening of the valve in commissurotomy. They found that commissurotomies could have been broader in men (71.4% of those with flaccid valves and 20% of those with fibrotic valves). They found good clinical results in both sexes (66.6% of those with flaccid valves and 33.3% of those with fibrotic valves in men, and 84.2% of those with flaccid valves and 100% of those with fibrotic valves in women). The authors concluded that: (1) the surgeon can obtain a good opening of the valves in patients of both sexes with pure mitral stenosis, even in fibrotic valves; and (2) in spite of the surgeon's statement that he was able to make a larger number of good commissurotomies in men with pure mitral stenosis, a smaller number of final good clinical results was obtained in such patients. The authors attributed this to the fact that men have greater fibrosis and more calcification, causing a final valvular inertia and rigid dysfunction, in spite of whether the surgeon could open the commissures.

Physician's Census.—The total number of physicians in Brazil in 1950 was 20,905. Of that number, 13,763 or 66% were living in capital cities. In 1950 there was one physician for every 2,488 persons, compared with one for every 2,947 persons in 1940. The secretary of the Brazilian Medical Association stated that, although there was an increase in the number of physicians, the number is still inadequate. It is estimated that by 1960 there will be one physician for every 2,000 persons. At present there are 22 medical schools in Brazil. The total number of students registered in these schools was 9,363 in 1952.

Dr. Moacyr Alvaro Honored.—At a special meeting of the Paulista Medical Association on Feb. 12, 1955, Dr. Moacyr E. Alvaro was awarded the gold medal of the Centro de Estudos de Ophtalmologia. He spoke on the recent trends in organized ophthalmology.

DENMARK

Late Results of Gallstone Removal.—Recent follow-up examinations of patients who have had gallstones removed continue to show disappointing results. Dr. J. M. Wollesen (*Nordisk medicin*, March 31, 1955) reports a series of 221 patients who were discharged after removal of gallstones in the period from 1939 to 1948; 19 had died of causes not connected with their gallstones. With one exception, they were included among the patients regarded as cured by operation. The follow-up examination was carried out from 1 to 13 years after the operation, and the patients were classified in two groups according to whether they were well after the operation; 27 were found not to have been cured by operation. The mean age of all the patients was 44 years when their illness began, 50 years when they were operated on, and 56 years when reexamined. The late results appear to be unaffected by the patient's age when operated on and the duration of his illness before operation. Simple cholecystectomy was performed on 152 patients and in combination with choledochotomy on 69 patients, the late results being about the same for the two operations. The interest of this follow-up investigation centers about the 27 patients who were not cured by the operation. In seven, stones may have been overlooked in the deeper bile passages. In a certain number of patients this is unavoidable. Among the patients not cured by operation four were suffering from chronic constipation and four others from dyspeptic symptoms; in four more no explanation could be found for the persistence of symptoms. The combination of gallstones with duodenal ulcer is common enough to warrant a careful examination for the latter as well as for the former. It is possible that the removal of the gallbladder may be the true cause of some postoperative symptoms.

Barbiturate Poisoning.—According to a report by the Danish health authorities, the number of patients with poisoning caused by agents such as hypnotics and carbon monoxide admitted to hospitals in Denmark in 1945 was 1,509. The corresponding figure for 1953 was 3,834. In the same period the mortality rate fell from 24.5 to 3%. Copenhagen in 1953 had a still lower mortality rate (2.1%), and the credit for this achievement is largely due to the centralization of cases of poisoning in the Bispebjerg Hospital, to which about 800 such patients are admitted every year. In *Ugeskrift for læger* for Feb. 17, 1955, Dr. Elisabeth Larsen has reviewed the experiences of this hospital during the first full four years (1950-1953) of its special work in this field. One of the barbiturates had been taken by 85%

The items in these letters are contributed by regular correspondents in the various foreign countries.

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of these patients. Only 3% of the cases of poisoning were due to morphine, whereas carbon monoxide accounted for 11%. During the last five years the formerly popular use of stimulants in treating these patients has been abandoned at the Bispebjerg Hospital. Thanks to this change of policy, pyrexia has ceased to impede recovery.

Treatment of Pulmonary Diseases with Tetracycline.—In view of the frequent and troublesome side-effects of chlortetracycline, a trial has been given with tetracycline at the Blegdam Hospital, Copenhagen, where in about three months 90 patients were given this antibiotic. The dosage was usually 250 mg. four times daily for adults and 250 mg. twice daily for children for six days. In her report on this subject in the *Danish Medical Bulletin* (vol. 2, no. 1, February, 1955), Dr. Alice Grüner notes that, among the 51 patients with pneumonia thus treated, there were only four in whom no effect was observed. The results were good in 44 patients and doubtful in 3. In four patients with chronic bronchitis the results were disappointing, with only one good result. The results in six patients with chronic pyelonephritis were also disappointing, as no benefit could be claimed in any of them. On the basis of ordinary clinical judgment and radiological findings, the conclusion could be drawn that tetracycline had an extremely good effect corresponding somewhat to that of chlortetracycline and oxytetracycline. The side-effects were slight, and the drug had to be discontinued prematurely in only one case.

Cancer of the Cervix Uteri.—In the *Danish Medical Bulletin* (vol. 2, no. 1, February, 1955) Dr. Kai Nielsen reviews the experiences of the Radium Center in Aarhus with regard to the influence of social factors on the prognosis for cancer of the cervix given a uniform, combined radium and x-ray treatment. His material consists of the 1,186 patients treated between May 1, 1940, and Dec. 31, 1948. After an observation period of at least five years, the social histories of 1,136 unselected patients were investigated with a view to ascertaining what part, if any, social factors play with regard to the prognosis. The patients were classified according to whether the disease was in one or the other of its four stages. The patients were interviewed by an experienced social worker with regard to such personal factors as income, housing, number of children, domestic work, and marital status. The five year survival rate was significantly lower for patients from the poorer classes than for those from better-off classes, irrespective of the stage of the disease. This difference was presumably due to the relatively poor opportunities for rest and convalescence after treatment available for the poorer classes.

ENGLAND

Infant Feeding and Diseases in Later Life.—Prof. B. S. Platt of the Human Nutrition Research Unit has suggested that errors in infant feeding might be the cause of disease in later life (*Brit. M. J.* **1**:179, 1955). In western countries many infants are never breast fed, or, if they are, weaning takes place early. Chemically there is an appreciable difference between human and cow's milk. There is, for example, six times as much calcium in cow's as in human milk, and this might well be a cause of hypercalcemia. Cow's milk, on the other hand, contains less lactose than human milk. Galactose, which is derived from lactose, is an essential constituent of the cerebrosides of the central nervous system and the mucopolysaccharides of connective tissue. Myelinization of nerve tissue continues until the fifth or sixth year of life. Platt suspects that when an infant is artificially fed on a "humanized" cow's milk preparation, which may supply only a third as much galactose as human milk, the composition of myelin may be affected. If insufficient galactose is available, cerebrosides containing glucose are formed in the body of the experimental animal. If such abnormal cerebrosides are present in the myelin of the infant, this might affect the subsequent health of the child. Galactose deficiency, with a change in the composition of myelin, may play a part in the cause of multiple sclerosis. In communities where breast feeding is usual, multiple sclerosis is rare, and where large quantities of carbohydrate are consumed in infancy, as in the West Indies, nervous diseases such as transverse myelitis are common. Animal experiments have shown that deficiency diseases in infancy, or even in utero, may affect the animal in later life. We may be reaping in medical practice and in the postmortem room today the errors of infant feeding methods that were prevalent 20 to 30 years ago.

Galactose is also a constituent of some components of ground substance and connective tissue; with glucose and mannose it is an integral constituent of the reticular fibers of connective tissue. The presence of galactose in collagen has been reported, and it has been claimed that there is some abnormality in this constituent in the collagen diseases. The artificial feeding of infants results in a deficiency of galactose, which may affect the nature, composition, and reaction to stress in later life of the extracellular matrix and connective tissue.

Management of Inoperable Cancer.—Despite advances made in the treatment of cancer, there are still many patients with incurable disease who need palliative treatment. A discussion on their management was recently held at the Royal Society of Medicine. H. T. Simmons of Manchester presented the surgeon's point of view. He said that heroic surgery is of doubtful value and seldom justifiable. Adrenalectomy and hypophysectomy have a place in the treatment of growths associated with the endocrine glands, but only half the patients obtain relief, and these operations should not be used indiscriminately. Perhaps in the future internal secretions will be suppressed by medical means. Certain operations have a palliative value, such as relief of intestinal obstruction by a bypass or colostomy, although the latter operation is seldom justified in an older person with inoperable rectal cancer, as it only adds another complication without relieving the distressing bleeding and tenesmus. Relief of pain is important, and short-circuiting operations that do not relieve pain and discharge probably do more harm than good. Metastases giving rise to symptoms can often be removed. Hormonal therapy is of value in the palliative treatment of cancer of the parasexual organs, but its effectiveness in any particular patient is unpredictable. Skin cancer requires palliative treatment only when the face is involved. Gastrostomy is not advisable in carcinoma of the esophagus, because the accumulation of saliva and inability to swallow distresses the patient. In carcinoma of the stomach palliative gastroenterostomy is rarely justified; the growth should be removed whenever possible.

The neurosurgeon can help the patient with incurable cancer, according to Prof. Norman Dott of Edinburgh, by relieving pain surgically and by preserving important neural functions threatened by the cancer. Metastatic cancer of the brain has increased in proportion to the increase in bronchial carcinoma. All patients over the age of 30 with progressive cerebral tumors should be investigated for primary growths elsewhere, particularly in the lungs. Not infrequently the cerebral metastasis is recognized first. Operation for the relief of pain is justified when there is an expectation of life of more than three months and when the pain is severe. Relief of pain can be accomplished by interruption of the pain-conducting pathways, so that pain stimuli are prevented from entering consciousness, and by leukotomy. Leukotomy does not abolish pain sensibility but abolishes its distress. A kind of chemical leukotomy can be produced by large doses of chlorpromazine. Neurosurgery is sometimes required to preserve neural functions threatened by tumor tissue, e. g., cranial decompression for cerebral metastases and spinal decompression to avert paraplegia. Murray Falconer, a neurosurgeon, disagreed with other speakers on the value of hypophysectomy for parasexual tumors. The operation has a low mortality and helps more than half the patients. The encouraging results make it difficult to say that there is a stage when this treatment should be withheld because the disease has become too advanced.

The internist's point of view was presented by C. J. Gavey of London, who said that hope should not be abandoned. Not all patients suffer from pain, but when this is present it should be relieved, because freedom from pain improves morale. Analgesics should be given continuously if need be, and the physician should not be afraid to give narcotics if they are needed. Demerol and methadone are often better than morphine, because they do not depress the patient as much, and chlorpromazine is useful in patients who are vomiting. Morphine should be used in

the terminal stages, although it is difficult to know when to start therapy, and, if possible, a dose of 22 mg. (⅓ grain) should not be exceeded. It is always difficult to tell the patient he has cancer, and it is always morally wrong to withhold this information if the patient requests it. If the patient wishes to be deceived, there is no harm in keeping up the deception. Most patients, however, accept the truth if it is imparted slowly and gradually. G. F. Abercrombie, a general practitioner, complained that consultants often deceive the patient, who is left in ignorance until the end. It is a mistake not to give the patient credit for having common sense and courage. Keeping the patient in ignorance puts the physician at a great disadvantage. The physician usually underestimates the ability of the patient to take a death sentence. P. Nathan of London took the opposite view, saying that the physician has no moral duty to reveal the truth and that there is a good case for the deliberate cultivated lie. Dr. Abercrombie said that the increasing nursing supervision required in the terminal phases often becomes impossible in the patient's own home and it is the duty of hospitals to readmit their patients in this phase. Unfortunately, they seldom do so and leave the patient to die at home. Professor Wells of Liverpool suggested that the palliation of cancer has so many aspects that a team of workers should be organized to deal with it. This was regarded with some misgivings by the others, who considered that the experts might not all agree.

Neglect of Disk Lesions.—Dr. James Cyriax of St. Thomas' Hospital, London, urges the manipulation of lesions of the nucleus pulposus immediately after they are diagnosed (*Brit. M. J.* **1**:140, 1955). Large numbers of patients with the diagnosis of disk lesions causing pain in the trunk or limb are seen in every hospital, yet not enough effort is being made to treat these patients actively. A lesion of the nucleus pulposus is a medical emergency, and manipulation should be carried out on the spot as soon as the diagnosis is made. This policy has been observed for years in the department of physical medicine at St. Thomas' Hospital. The patient is not only relieved of his symptoms there and then but stretching of the posterior ligament is reduced to a minimum, and since this ligament forms the only bar to further protrusion, every effort should be made to spare it the prolonged pressure of continuing displacement, especially at the cervical and thoracic levels, where the cord is in danger. Moreover, nearly all lesions of the nucleus pulposus set up pain in the trunk before root pain supervenes; hence, if reduction is carried out at this stage, increased protrusion leading to root pressure is avoided. At St. Thomas' Hospital manipulative reduction and traction is accomplished by the physiotherapists and students. Seldom is it necessary for the physician diagnosing the condition to do it himself.

There are very few hospitals in Great Britain where a minor disk subluxation is manipulated back into place while it remains minor and easy to reduce. Epidural local analgesia as a prelude to treatment or manipulation that is likely to be painful appears unobtainable as an immediate outpatient measure in nearly every hospital; only recumbency, a plaster jacket, or operation remain. As a result the patients go to unqualified manipulators or osteopaths. Such a state of affairs would not be tolerated in any other branch of medicine, particularly as the patient pays the osteopath and not the state-employed physician. If manipulation of the spinal joints were restored to the medical sphere, patients would not only be relieved at once and the liability to further trouble reduced to a minimum but much abuse would be avoided because visits to the unqualified practitioner would cease. If, however, osteopaths continue to treat the disk lesions neglected by physicians, they will ultimately get state recognition. If a survey were made, what hospitals could answer the following questions satisfactorily: What arrangements exist in your outpatient department for spinal manipulation? Manipulation under anesthesia by the orthopedic surgeon on inpatients only touches the fringe of the problem, as the existence of some 2,000 lay manipulators demonstrates. Furthermore, after a patient has visited several physicians, has failed to obtain relief for his disk lesion, and finally gets relief from an unqualified manipulator, he might argue that the physicians were guilty of negligence and seek his remedy in the courts.

Salaries of Civil Service Medical Officers.—For some time there has been dissatisfaction over the rates of pay of the 600 medical officers directly employed by the Ministry of Health and other ministries. In 1948, the year the National Health Service Act was implemented, the Treasury was asked to apply the findings of the Spens Reports (on which the salaries of specialists and medical practitioners were based) to the medical personnel of the Civil Service. The Treasury refused to do this, and its failure to carry out an early review of the salary scales recommended by the Howitt Committee, which was appointed to examine the rates of pay for medical officers in the Civil Service, resulted in much friction between the Treasury and the British Medical Association. The *British Medical Journal* refused to accept all notices of civil medical appointments under government departments. This ban was only lifted when the Treasury agreed to increase the pay of Civil Service medical officers, subject to recommendations of the Royal Commission on the Civil Service. The Civil Service Medical Officers Joint Committee, which is a joint committee of the British Medical Association and the Institution of Professional Civil Servants, has now submitted evidence to the Royal Commission. The salary scales proposed are about 50% above the existing rates of pay for those at present receiving $6,440 or more a year and 30 to 40% more in the case of those receiving less than this amount. The new rate of pay proposed for the chief medical officer of the Ministry of Health is $16,800 a year. Chief medical officers in the various ministries would receive a little less than this and deputy chief medical officers, $12,600 a year. Senior medical officers would get $8,680, and ordinary medical officers would be on a salary scale from $4,480 to $8,040 a year.

The Joint Committee said that it saw no reason why a physician employed by one government department should be paid any less than another serving the state in the National Health Service, in either a hospital or general practice. The committee considered that the chief medical officer of the Ministry of Health should receive a salary commensurate with that of a senior specialist working within the National Health Service and receiving an income from private practice. This was assessed at $16,800 a year. The salary of a deputy chief medical officer was considered to be about three-fourths of this. Other salaries were equated to those paid to physicians of similar standing doing full-time hospital work.

Appointments in Outpatient Departments.—Following local criticism of the lack of a proper appointment system at certain hospitals, the Manchester Regional Hospital Board has examined the present outpatient practice in all of its general hospitals. In its report the board is emphatic in stating that an outpatient appointment system should be universal, with the possible exception of hospitals isolated in rural districts, and it hopes that the specialists attending the hospitals in the region will cooperate in operating it. Appointment systems of one kind or another will be employed in all hospitals in the Manchester region. Dealing with the widely held view that appointment systems lead to lengthening of the waiting time for an appointment, the board does not believe that this need be the case. With efficient organization of all parts, the appointment system should work to the satisfaction of physician and patient. If an appointment system does not seem to work, the reason should be sought. As the needs of hospitals vary, the board has avoided recommending any particular form of appointment system, such as the individual type, when a patient is asked to come at a particular time, or the block type, in which a group of patients are given the same appointment and are seen in quick rotation.

The report of the board discusses the punctuality of the staff, and, while recognizing the difficulty of operating a medical service on an exact schedule, it asks that cases of repeated unpunctuality be reported. It also points out that patients, as well as staff, can be unpunctual and quotes an analysis of the attendances by appointment of 198 patients, of whom only 48 attended at the right time, 42 attended up to an hour too early, 68 attended up to 1½ hours late, and 20 failed to attend at all. The board says that there is no more effective method of improving hospital service public relations than a well-organized and sympathetically run hospital outpatient department.

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Treating Patients in the Home.—Dr. J. L. Burn, Health Officer for Salford, believes that more efforts should be made to treat the patient at home. Psychological, medical, and financial reasons favor the complementary use of the home and the hospital in the treatment of the sick. Domiciliary visits by specialists, who are an integral part of the National Health Service, keep many patients out of hospital and also insure that those in need of hospital treatment get it without delay. Earlier discharge of patients from the hospital is now arranged in many areas, although some hospitals hesitate to do this as a routine, as they are not always certain of the standard of home care available. District nurses could be used more fully, particularly in the care of sick children. At the moment too many are spending their time nursing older persons. Pediatricians are not called in consultation as frequently as other specialists, and often there is some delay in calling in the general practitioner to see a sick child. The visiting nurse should pay more routine visits to babies in neglected areas and should press the parents to call a physician early when a child is sick. She should also have more opportunity for official collaboration with the district nurse, who in turn should be in close touch with the family physician. All three should have frequent discussions at the local health department.

The district nurse can observe the needs of all the families that she attends. She should be able, when necessary, to enlist the aid of the family physician, visiting nurse, home help, sanitary inspector, and any other person available under the National Health Service. In some of the health centers, of which there are very few at present, the health team (physician, home nurse, midwife, and visiting nurse) work in close collaboration. The nursing service would be more efficiently used if less highly skilled persons were employed on routine tasks, such as making beds and giving baths. Another way of saving time would be for the health department to run a central syringe service, supplying physicians and nurses with sterilized syringes and perhaps other sterilized equipment. A clinic might also be organized where the nurse could give all ambulant patients any injection needed. At present she wastes much time visiting the patients to give them their injections. The nurse and the physician have opportunities for general health education of the public.

Birmingham Emergency Accident Plans.—The necessity for a large-scale emergency accident organization to deal with catastrophes has been emphasized by the overturning of the York-Bristol express at Sutton Coldfield with a large death and accident toll. The Ministry of Health has suggested to hospitals and local authorities some ways in which their organizations for dealing with major accidents might be improved. Birmingham, which has a well-equipped accident hospital, has taken the lead and drawn up an emergency plan for large-scale accidents, with the cooperation of the police, the ambulance services, the general practitioners, industrial physicians, and the voluntary organizations. A major catastrophe is defined as one involving 50 or more seriously injured casualties, or one that is determined as such by the duty officer at the fire and ambulance control center in the light of the circumstances. The duty officer at the control center therefore decides whether to put the plan into operation, although he will consult when necessary with the physician in charge of casualty services, who will be on the spot as soon as possible. When a catastrophe, such as a big fire or train accident has occurred, the hospital services will provide a team of physicians and nurses, with equipment to set up a first-aid post at the scene of the accident, and a physician in charge of casualty services, who will organize and direct first aid on the spot. Simultaneously, the police will send two radio-equipped automobiles and establish an incident post, which will be in radio communication with the control center and the central police center. The police will also have a limited amount of first-aid equipment. They will be responsible for recording names and addresses of the injured and for setting up mortuary accommodation near the scene.

The physician in charge of casualty services, who will be a senior surgeon with wide experience in accident work, will be in contact with the senior police officer and the senior fire and ambulance officers. His principal duty will be the organization and direction of all first-aid services. At the control center there will be a medical coordinating officer working in conjunction with the police, the fire and ambulance service, the St. John Ambulance Brigade, the Red Cross, and the hospital services. Although general practitioners and others may be on the scene a short time after the disaster, the Birmingham accident authorities decided that hospital first-aid teams should support them. There are 4 teams, each composed of a physician and four nurses, on immediate call at hospitals in the accident area, and another 10 teams are available within one hour, with all necessary equipment.

The blood transfusion service will organize a flying squad, and an industrial physician with, if possible, a first-aid team from a factory nearby will also report at the incident post. Three general practitioners in the neighborhood will be asked to give help in their area and another three, to hold themselves in readiness. The Birmingham plan includes details for mobilizing such voluntary services as the St. John Ambulance Brigade and the Red Cross. Hospitals will have beds available by sending home patients who can be nursed at home if necessary.

It is always difficult to decide how much resuscitation should be given before removal of the injured to a hospital. Dr. William Gissane, the director of the Birmingham Accident Hospital, has discussed this with his colleagues. They have considered whether it is more useful to set up a casualty clearing station with resuscitation measures at the scene of a serious accident or whether it is better to arrange for speedy evacuation to a hospital. It was thought that if a major disaster occurred at 5 to 8 miles from a well-equipped hospital, evacuation to that hospital should be done as soon as possible. Once at the hospital, resuscitation and treatment would be quickly available. If, however, the hospital was 10 miles or more away, it was felt that this was a case for setting up a casualty clearing station on the spot, although this had practical difficulties. It would always present an organizing problem to set up such a station under adequate medical control. Dr. Gissane said that, to justify more resuscitation on the spot, a casualty clearing station would have to be set up within 40 minutes of the accident and this would involve difficulties of organization. An accident surgeon of wide experience should be there to assess the urgency of each case. Dr. Gissane said that he hoped first aid might be simplified by the use of a new stretcher made of Fiberglas lined with foam rubber that was on trial at the Birmingham Accident Hospital. This becomes molded to the body, so that when the patient is placed in it the limbs are effectively splinted. It has also been suggested that a helicopter service might be used to evacuate casualties when a major catastrophe occurs well away from any large town or hospital.

Bequeathing the Human Body.—Since Annette Mills, a television star, bequeathed her body for the advancement of surgery recently, the Inspector of Anatomy of the Ministry of Health has had over 200 requests from persons asking how they may bequeath their bodies for dissection after death. There is a great shortage of bodies for anatomic and surgical purposes in the hospitals and medical schools. Before 1945-1946 only about 20 bodies a year were bequeathed for dissection. After that year, owing to publicity, bequests have increased. Unless these continue, hospital and medical schools will have to depend in the future on unclaimed bodies or the bodies of paupers, as they did in the past. The British Medical Association has also received numerous inquiries from interested persons since publicity was given to the Annette Mills bequest. The association has prepared a leaflet explaining how a person who wishes to leave his body for dissection can insert a clause in his will to this effect or leave a written request with his executor or family. Close relatives can, if they wish, annul this request on the death of the person making it. The leaflet also gives details of the procedure to be followed for the interment of the remains. One physician has stated that the medical profession should take the lead, all physicians bequeathing their bodies in their wills to the hospitals unless their next of kin object. This would go far to remedy the present shortage of bodies. Much interest has also been aroused in the Corneal Grafting Act of 1952, under which it is possible for a person to bequeath his eyes after death for the purpose of corneal grafts by a verbal declaration before two witnesses or in writing. Details of this act are also given in the British Medical Association's leaflet. Mr. B. W. Rycroft, an ophthalmologist of the Corneo-Plastic Unit, Queen Victoria

Hospital, Sussex, says that, as a result of a letter from Sir Reginald Watson-Jones, the orthopedic surgeon, to the *Times* newspaper, on bequeathing eyes for corneal grafting, a large number of letters and inquiries have reached the hospital. Corneal tissue is urgently required for grafting. Many people in Britain have recovered their sight, when loss of it has been due to a corneal defect, after corneal grafting from eyes provided by bequests.

The Doctor's Telephone.—A London executive council has ruled that a physician working in the National Health Service is not required by his terms of service to provide a telephone at his residence or office, and, if he has a telephone, he is not obliged to let it be available to his National Health Service patients. This ruling arose out of a complaint of a patient that she waited all day for the physician to visit her 8-year-old daughter who had tonsillitis. She could not call him because he had no telephone, and she could not go to his office because she had to look after the child. When the father arrived home in the evening another physician was found and the child treated as a private patient. The Medical Services Committee held an inquiry. The physician admitted that he had a telephone but that it was not available to National Health Service patients. The committee was unable to find that the physician did not comply with his terms of service. While it disapproved of his conduct, in its opinion he was not required by his terms of service to provide a telephone. One member of the committee said that patients should insist on being on the list of a physician who was accessible by telephone. The statutory terms of service are not exclusive. The executive council is entitled to add to them. This can be done even after the physician has entered into his contract, provided the Minister of Health consents.

Dr. C. H. Hampshire.—On Jan. 25 the death of Dr. C. H. Hampshire occurred; he, more than any other person, can be considered responsible for the success of the World Health Organization's work on the unification of pharmacopeias. He was appointed chairman of the Technical Commission of Pharmacopeial Experts set up by the League of Nations in 1937. After World War II he was appointed chairman of the Expert Committee on the Unification of Pharmacopeias. Four years later the first volume of the International Pharmacopeia was published—an amazing achievement in such a relatively short space of time, for which much of the credit must go to Dr. Hampshire. In 1929 he became secretary of the British Pharmacopoeia Commission, a post he held for over 20 years. He was responsible for the radical revision of the British Pharmacopoeia that characterized the 1932 edition and that was universally acclaimed as a model of its kind.

ITALY

Surgery of Mitral Defects.—At a meeting of the physicians of the Sannio region in October, Professor Dogliotti of the University of Turin said that the idea of opening up the stenotic valvular barrier appealed first to pathologists who had become aware of the fact that the entire life of the patient was undermined by this one impairment. The progress made in the fields of thoracic surgery, anesthesiology, and antibiotics has paved the road for the attack on mitral stenosis. The problem was solved when the right index finger replaced surgical instruments. It has since been proved that it is possible to introduce this finger into the stenotic orifice for investigative as well as for surgical purposes.

About six years ago, when Professor Dogliotti performed his first cardiac operations, he became convinced it was necessary to set up a center where there could be a greater cooperation between the physician and the surgeon. This would result in greater diagnostic accuracy and would facilitate the decision on the exact therapeutic indication. Through this center the constant progress made in the field of cardiac surgery could be brought to the attention of the general practitioners. One such center has been established in Turin, and, in view of the large number of Italians with heart disease, it is hoped that others like it will soon be opened. The speaker then listed the qualities that are indispensable to the surgeon who wishes to dedicate himself to cardiac surgery. Not one such operation should be undertaken by a surgeon who is not conscientiously prepared, because, besides risking a grave failure, a bad service is rendered to cardiac surgery. Before deciding whether a patient treated in a cardiosurgical center should be operated on, a general medical examination by a cardiologist, which would include electrocardiograms, roentgenograms, intracardiac catheterization, and angiocardiography, if indicated, must be given. It is important to determine also the degrees of pressure in the heart cavities. Great thought should be given to the intervention and to its results when there is a pulmonary barrier that cannot be modified. After these studies have been completed, the operation can be undertaken after a period of preparation that varies according to the type of defect present and the underlying pathological process.

A personal method of Professor Dogliotti for evaluating the degree of aperture of the orifice consists in relating the finding to a chalk model of the index of the right hand. In his series of over 400 patients with mitral stenosis on whom he operated, he stated that although the mortality rate in the first 50 was 12% it decreased to 1% in the last 250 patients. This indicates that experience and a correct indication are significant factors. Today in the uncomplicated forms the risk is close to zero.

Epileptic Equivalents.—At a meeting at the surgical clinic of the University of Pisa, W. Penfield of the University of Montreal said that experiments carried out in Canada indicate that memory is situated in the temporal lobe. By applying electric stimulation to various points of the temporal cortex in epileptic patients, he was able to reawaken in them old and recent memories. The practical conclusion that was derived from these experiments was that the removal of some parts of the cortex of the temporal lobe may benefit patients with masked epilepsy. Professor Boschi of the University of Modena said that the stirring up of single and precise memories by means of stimulations that, like those produced by a macroscopic electrode, are relatively quite diffuse needs an interpretation other than that of the reawakening of mnemonic images located in that part of the cortex. He believes that the stirring up caused by Penfield's experiments acts through a reflex mechanism or a mechanism of association. This leads one to believe that the psychological function in general and with it the memory have an extensive location in the cerebral cortex.

Professor Boschi's concept of consciousness presupposes the existence of a metaphysical problem. By consciousness he means the subjective in psychological phenomena, a psychological phenomenon being any nervous reaction that has in itself the capacity of assuming consciousness. The possibility of provoking experimentally psychological responses to the stimulation of certain temporal locations assumes special importance, also from the therapeutic standpoint, if one recalls the concept of the mesencephalon. This is the area in which the coordinating functions of the vegetative life of the organism and the instinctive and automatic reactions take place. In the mesencephalon are also parts of the temporal lobe, in which may be located those primary signs that characterize certain manifestations called psychological epileptic equivalents.

Toxic Goiter and Myxedema.—Prof. Nicola Pende in an address to the medical and surgical societies of the Silento area stated that any endocrinopathy can have at least six pathogenetic mechanisms according to whether the primary factor is in the gland, the diencephalic nervous centers, the hypophysis, another correlated gland, the metabolism of the substance that serves for the molecular construction of the hormone secreted by the gland that is being considered, or the peripheral effector organs that regulate the amount of secretion of such a gland. The diencephalic centers, the hypophysial hormones, and the other glands may relate with each other through the hemocrine route, the neurocrine route, and the route of the system of the hypophysial veins. The speaker did not agree with those who believe that thyrotoxicosis is always a primary diencephalohypophysial disease rather than a primary disease of the thyroid associated with diencephalic symptoms. He admits that the main symptoms

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of the disease, such as the increased basal metabolic rate, debility, and tachycardia, constitute specific thyropathic symptoms, as does the lack of disturbances of the genital area, of thermogenesis, and of sleep. The characteristics of the diencephalohypophysial and neurothyrotropinic aspects of the disease are, however, a slight increase of the basal metabolic rate, possibly the presence of adiposity, disturbances of the genital area, and insomnia. There is in addition a marked exophthalmos, with disturbances of the ocular motility. The characteristic of hypophysial or hypothyrotropinic myxedema is the coexistence of an adrenal and genital insufficiency together with the thyroid insufficiency. There is intolerance, sometimes fatal, to thyroxin, whereas the thyrotropinic therapy combined with adrenal and genital organotherapy is useful. The treatment of choice for diencephalohypophysial thyrotoxicosis is irradiation of the thyroid, the diencephalon, and the cervical sympathetic ganglions. The speaker excludes thiouracil preparations entirely.

Agreement Between Physicians and Medical Insurance Institute.—An important controversy that had been going on for several months between Italian physicians and the National Institute for Medical Insurance was finally settled when high officials, including the Minister of Labor and Social Insurance and the president of the National Federation of the Order of Physicians, intervened. The physicians and the institute reexamined and reorganized all the material relating to the assistance that will be given by the national insurance fund to the insured person in case of illness. From now on, such assistance will be either direct or indirect as the worker chooses. In the direct form of assistance the institute will provide a general practitioner or a specialist, a hospital, and drugs. The patient will have the right to choose the general practitioner from rosters available at the various provincial centers of the Order of Physicians. Any physician can place his name on these lists if he wishes to do so. Salaries to physicians for their services to the insured workers were increased by 15%. Assistance by a specialist on an outpatient clinic basis will be given at special centers that the National Insurance Institute will set up. In the indirect form of assistance the institute will reimburse the insured worker for his doctor and drug bills on the presentation of such receipted bills.

Control of Narcotics.—The Commissioner of the Public Health Service distributed a circular letter in which a new law (Oct. 22, 1954) governing the production, sale, and use of narcotics was discussed. According to this new law, the commissioner will compile a list of habit-forming preparations. Permission grants, which will be given by the Commissioner, will be needed for growing poppy and other plants from which narcotics can be extracted. Every quarter the firms that produce narcotics must send to the commissioner a detailed report on the nature and use of the raw materials received and on the products that were derived from them. These firms will not be permitted to send to physicians and veterinarians samples of narcotics under any form. Before selling narcotics, the pharmacists must ask the buyer for some identification and must write on the medical prescription the kind of identification presented.

Anticoagulant Therapy.—At a meeting of the Society of Medical Culture of Novara, Professor Campanini stated that anticoagulant therapy had been used for one year in the outpatient clinic in treating patients with arteriosclerosis localized in the extremities, the myocardium, and the brain. It is necessary to make sure that there are no contraindications and that the patient returns frequently to the clinic for a blood test. During the first week of treatment he should be seen every day; thereafter once a week is sufficient. It is not possible to set a general standard of dosage. The drug used at the clinic is ethyl biscoumacetate, administered in doses of 900 mg. on the first day and 600 mg. on the second. The patient is then given a blood test, and the successive daily doses are prescribed according to the results of this test. When anticoagulants of the dicumarol type are used, the coagulability is checked by determining the prothrombin time; in addition the coagulability of the blood in toto is checked according to the method of Losner and Wolk.

Professor Franzini reported encouraging results with anticoagulant therapy in 16 patients with a peripheral arteritis obliterans of arteriosclerotic origin. They were all treated with anticoagulant substances alone. The combination of this treatment with the intra-arterial administration of insulin proved useful to some patients with diabetes. When the signs of the functional alteration of the peripheral circulation (intermittent claudication and decubitus pains) became attenuated or disappeared, the administration of the dicumarol-like substances was discontinued and heparin was given, mainly to take advantage of the vein-dilating and antilipoprotein properties of this preparation. Of the 16 patients that were thus treated, only 2 had to undergo amputation of the impaired extremity. A notable improvement, which was still present after several months, was obtained in 65%. No complications were observed and no drug intolerance.

Statistics on Morbidity.—The Central Institute of Statistics discloses that, in 1954, 13,335 cases of diphtheria were reported, as compared with 15,779 in 1953; 3,365 cases of poliomyelitis (4,995 in 1953); 25,635 cases of typhoid and paratyphoid (27,128 in 1953); 1,089 cases of epidemic cerebrospinal meningitis (1,198 in 1953); and 8,606 cases of undulant fever (9,349 in 1953). In the instance of tuberculosis, a comparison between the cases that were reported during the last 11 months of 1954 and those that were reported in 1953 shows that there was in 1954 a decrease of 1,344 cases. During the same period the cases of influenza decreased by 42,468. On the other hand, the cases of amebic dysentery, infectious spirochetal jaundice, measles, smallpox, mumps, and acute primary hepatopathy have increased.

JAPAN

Symposium on Surgery of the Pancreas.—At a meeting of the Japanese College of Surgeons in Okayama in April, 1954, Dr. Jiro Suzuki of the Chiba University Medical School said that advanced carcinomas of the lower portion of the esophagus or the cardia or fundus of the stomach for which radical operation is no longer feasible are frequently encountered. An attempt to remove the malignant lesion en masse including the spleen and the tail of the pancreas has been made in 73 patients. The tail of the pancreas is resected perpendicular to the lower margin of the pancreas through a point where the middle colic vessels cross that margin, thereby facilitating the removal of the involved retroperitoneal lymph nodes. The operative mortality in this series was 2.9%, and the results as judged by postoperative follow-up indicate a high degree of success.

Fat Metabolism.—Dr. Yoshio Onno of the Osaka University Medical School has studied fat metabolism after pancreatic resection in dogs. When the pancreas has been totally removed, the animals are apt to show fatty change of the liver even with adequate insulin administration, and most of them die within 10 days. The hepatic function in these dogs is greatly impaired. If only 80% of the pancreas is removed, the island cells in the remaining portion regenerate and the liver cells partially recover from their fatty change. Simultaneous splenectomy prevents the development of pathological lipotrophy.

Results of Pancreatoduodenectomy.—Dr. Reizaburo Suzki of the Tohoku University said that pancreatoduodenectomy is one of the unexplored fields in surgery. The mortality is high. The operation is extremely difficult because (1) it is performed simultaneously on the stomach, duodenum, bile ducts, and pancreas; (2) the bile duct and the remaining pancreas must be reconstructed; (3) the portal vein and superior mesenteric vein are easily injured and cannot be ligated and divided; (4) since jaundice does not appear until late in the course of the disease, the icteric patient often does not visit the surgeon until the optimum time for operation is past; and (5) secondary hepatic injury is expected in all cases. Although postoperatively the digestion and absorption are improved, the return of these functions to normal cannot be expected. In a series of 30 patients, 13 had carcinoma of the head of the pancreas; 5 had carcinoma of the common bile duct; 6 had chronic sclerosing pancreatitis; and 6 had pancreatic metastases from cancer of the stomach. In operating special care is taken to avoid injuring the portal vein.

The circulation should be preserved insofar as possible for the sake of the function of the remaining pancreas. Anastomosis of the portal vein and insertion of a polyethylene tube connected with the vein graft has been tried. The direct mortality up to 1952 was 50%, but it has since been reduced to 18%. The deaths in the latter period are due to a liberalizing of the indications. If patients are carefully selected for the operation, the direct mortality should presumably be reduced to the vanishing point. No patients in this series lived more than one year after the operation.

Total Pancreatectomy.—Dr. Ichio Honjo of the Kyoto University has performed eight total pancreatoduodenectomies, including one on a patient who had lived a healthy life for three years after the operation when last seen. In patients in whom total pancreatectomy must be performed, the duodenum is resected because there is the possibility of necrosis of the duodenal wall if the pancreas alone is removed. The presence of cancer is an added reason for duodenectomy. To evaluate the efficiency of the gastrointestinal tract, the amounts of organic constituents (protein, fat, and carbohydrates) in the feces are compared with the amounts ingested. After the operation the digestion was found to be so severely impaired in dogs that the feces resembled vomitus. In spite of the administration of pancreatin and methionine, the absorption rate of carbohydrate dropped about 20% and that of protein about 54%. The absorption rate of fat varied widely and in the worst cases was found to be negative (more fat present in the feces than in the diet), indicating that a part of the fat in the feces was endogenous. When pancreatin and methionine were not given, even lower values were obtained. Digestion and absorption tests were made on three patients. Although the average absorption rate of protein and fat dropped 25 and 43%, respectively, the rate for carbohydrate was maintained at an almost normal value. From these data it is assumed that man retains a much better capacity for absorption after total pancreatoduodenectomy than does the dog. This capacity remained unchanged in patients one year after the operation, indicating a lack of any compensatory mechanism.

The cholesterol-ester ratio was determined in three patients postoperatively. The first patient was still living and well three years after the pancreatoduodenectomy without the administration of any medicament except insulin. The serum cholesterol-ester ratio was within the normal range throughout the postoperative course. There seems to be no possibility of fatty change developing in his liver. The second patient had been suffering from obstructive jaundice of three months' duration and showed a marked disturbance of liver function at the time of admission. After the operation the serum cholesterol-ester ratio returned to normal and its level was maintained for about 30 weeks, but, because of progressive hepatic cirrhosis, severe infection of the biliary ducts, and the development of a jejunal ulcer, the serum cholesterol-ester ratio began to fluctuate and decreased gradually. The patient died about one year after the operation. The third patient died of gradually increasing anorexia and emaciation five months after operation, in spite of the administration of methionine, vitamin B_{12}, and folic acid. The serum cholesterol-ester ratio began to decrease when the patient's general condition deteriorated. At autopsy this patient was found to have generalized tuberculosis with cavities in the left lung. Fatty change was found in the liver only in the last patient; none was detected in the other two patients or in three more patients whose livers were examined at autopsy. Thus fatty change was found in only one of six patients who survived more than one month after total pancreatoduodenectomy.

Insulin Dosage.—Some authors have stated that in dogs that have had their whole pancreas removed the dose of insulin should be reduced day by day postoperatively to avoid hypoglycemia. They interpreted this phenomenon directly as the increase in sensitivity of animals to insulin and also stated that this sensitivity was characteristic of the development of fatty change in the liver. The speaker injected a certain amount of insulin daily in dogs that had had their pancreas removed to keep the level of the fasting blood sugar at about 200 mg. per 100 cc. in the early morning. In 26 dogs observed for more than three weeks postoperatively it was necessary to reduce the insulin dose in only 6 animals. Fatty change developed in the liver of only one dog. It seems, therefore, incorrect to explain this phenomenon solely on the basis of fatty change. In six patients in whom total pancreatoduodenectomy had been done the blood sugar level was determined for more than one month after operation. One patient who was in good health three years after the operation constantly received about 30 units of insulin per day with no sign of hypoglycemia. The insulin dose of the other patients was reduced when such severe complications as jejunal ulcer, infection of the biliary ducts, hepatic cirrhosis, recurrence of cancer, and aggravation of tuberculosis occurred. These observations in man indicate that the dose of insulin need not be reduced after total pancreatoduodenectomy as long as an adequate food intake is maintained.

The insulin test was used to estimate the sensitivity of the body to insulin at a given time. Insulin was given intravenously to a fasting dog in which total pancreatectomy had been done and the blood sugar was recorded at certain intervals for four hours after the injection. In this dog the time required to reach the lowest level and the time required to return to the previous level was much longer than in normal dogs. From the determination of the assimilation index, which shows the grade of sensitivity, we learn that the index has a lower value in dogs in which total pancreatectomy has been done than in normal dogs, that is to say, the degree of insulin sensitivity was decreased after the operation. Insulin was given subcutaneously several times to a patient in whom total pancreatoduodenectomy had been done, and the blood sugar was determined as in dogs. The blood sugar curves thus obtained were similar to each other and showed a marked difference from those of normal persons. Although the velocity of the decrease in value of the blood sugar was slight, the level of the blood sugar steadily fell and sometimes signs of hypoglycemia occurred. As we do not see hypoglycemia after insulin injection in normal persons, we are apt to interpret this phenomenon as being caused by the increase of insulin sensitivity in persons in whom total pancreatectomy has been done, but the truth lies in the fact that both man and dog become somewhat insensitive to insulin after total pancreatectomy.

To investigate the disturbed balance of postoperative sugar metabolism the speaker examined the histological findings of the anterior lobe of the pituitary. The number of eosinophils and basophils was markedly reduced in dogs after pancreatectomy. The same findings were observed in a man at autopsy. These findings indicate that the endocrine function of the pituitary decreases following pancreatectomy. The amount of insulin required after total pancreatectomy is unexpectedly small compared with that required in endogenous diabetes. Moreover we usually ascribe the genesis of insulin-resistant diabetes to the hypofunction of the pituitoadrenocortical system. The reason we do not need to use a large amount of insulin for the treatment of postoperative diabetes in these patients is that the endocrine function of the anterior lobe of the pituitary gland is lowered after total pancreatectomy, although the disappearance of another hormone of the pancreas, glucagon, must be considered. Postoperatively decreased insulin-sensitivity is explained by the fact that the numerically decreased, yet still existing, chromophil cells continue to fulfill their function in the absence of the pancreas. Postoperative hypoglycemia that appears sometimes in patients undergoing a prolonged fast may be due to undernutrition, particularly in the liver, caused by the decreased efficiency of the gastrointestinal tract.

Jejunal Ulcers.—In dogs in which total pancreatoduodenectomy has been done, jejunal ulcers are likely to develop, particularly at the site of the gastrojejunal anastomosis, and these dogs may die of severe hemorrhage or perforation of the ulcer; 19 of the 26 dogs in this series suffered from ulcer formation. In this regard there was no difference between the dogs that were given pancreatin and methionine postoperatively and those that were not. The percentage of ulcer formation was not influenced significantly by whether the antrum of the stomach was resected completely or not. The dogs were divided into groups of those that did not show hypoglycemic shock through the postoperative course and those that did. Ulcers developed in all dogs that showed hypoglycemic shock, and those in which ulcers did not develop belonged to the group in which hypoglycemic shock did not occur. Total pancreatectomy was then performed on dogs without resecting the duodenum, and these

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dogs were divided into two groups—those that were given a small dose of insulin maintaining the level of the blood sugar constantly above normal and those that were given a large amount of insulin allowing occasional hypoglycemic shock. Postoperative jejunal ulcer did not develop in the former but developed in 33% of the latter group. These findings indicate that the development of jejunal ulcer may be prevented by maintaining the level of the blood sugar relatively high above normal after total pancreatoduodenectomy.

Gallbladder Resection.—Extirpation of the gallbladder at the time of choledochojejunostomy in dogs markedly reduced the rate of infection of the biliary system. After ligation of the ductus choledochus, the bile stagnates in the blood stream and the level of the serum bilirubin rises. If the gallbladder is removed concurrently with choledochojejunostomy, the serum bilirubin content rises much faster than before because of the bile-concentrating capacity of the gallbladder. The speaker performed a choledochojejunostomy on a dog and determined the value of the serum bilirubin. The level of the serum bilirubin rose faster than in the previous animal in spite of the existence of the gallbladder. These results indicate that the gallbladder can no longer display its normal activity of bile concentration after choledochojejunostomy. For this reason extirpation of the gallbladder should be done concurrently with pancreatoduodenectomy in order to remove the focus of infection.

Calcium Metabolism.—The speaker also studied the calcium metabolism after total pancreatectomy, as he had seen one case of tetany after operation. He gave a test diet that contained a certain amount of calcium to normal dogs and to dogs in which pancreatectomy had been done and compared the amount of calcium excreted in the feces of the two groups. The amount of calcium excreted in the feces of the dogs in which pancreatectomy had been done increased markedly and sometimes exceeded the amount of intake. Nevertheless, the level of the serum calcium was almost within the normal range in most of the dogs in which total pancreatectomy had been done. Moreover, the level of the diffusible serum calcium that probably is physiologically active was found to be within the normal range until nine weeks after the operation. Clinical signs of tetany, therefore, did not appear in the dogs throughout the first nine postoperative weeks.

Next the amount of calcium contained in the ribs of the dogs at various stages after the operation was determined. It was found that the amount of calcium contained in the ribs of the dogs in which pancreatectomy had been done was from 20 to 50% less than the average normal value during from 3 to 12 weeks after the operation. Osteoporosis was found on histological examination. The fact that the level of the serum calcium was maintained within the normal range in spite of the excretion of a large amount of calcium in the feces may perhaps be explained by the fact that the bone calcium was rapidly transported to the blood stream. One patient in the speaker's series revealed symptoms of tetany eight months after the operation and at the same time showed a marked decrease of the serum calcium, but this patient recovered soon after his calcium intake became adequate. As a man preserves a better efficiency of the gastrointestinal tract than the dog after total pancreatectomy, one cannot discuss the calcium metabolism in man as analogous to that in dogs, but the possibility of a calcium deficiency in man after the operation should not be ignored.

Although the source of serum diastase under normal conditions has been investigated, it is still unknown. The serum diastase in the animals used by the speaker decreased somewhat after total pancreatoduodenectomy but never to zero. In man, however, the serum diastase disappeared completely, even if transiently, about two weeks after the operation. This indicates that, even in the physiological state, the pancreas plays an important role as the source of serum diastase.

One patient complained of a transitory decrease in visual activity about eight months after total pancreatoduodenectomy, and at the same time it was noted that the value of his serum vitamin A was below the normal range. After operation the value of the serum vitamin A in both dog and man decreases to below the normal range. When fat-soluble vitamin A is given orally to a dog that has been subjected to pancreatectomy, it is poorly absorbed, but water-soluble vitamin A is easily absorbed. The speaker determined the value of serum vitamin A at intervals after the intravenous injection of water-soluble vitamin A and concurrently estimated the amount contained in the liver. Considering the data acquired from the normal dogs and those in which pancreatectomy had been done, it is reasonable to presume that the destiny of vitamin A that enters the blood stream of dogs subjected to pancreatectomy does not much differ from that of normal dogs. In other words, the tissues of the dog subjected to operation can utilize vitamin A that is injected into the body as adequately as the tissues of normal dogs.

Pancreatoduodenectomy.—In 1949 Dr. Hazime Yoshioka of the Tokyo Metropolitan Police Hospital reported two cases in which the head of the pancreas together with the duodenum were successfully removed. Since then he has performed this operation on 44 more patients. He found that diabetes did not occur when the pancreatic remnant was more than 20% of its original weight but that the carbohydrate metabolism was suddenly disturbed if the remnant was less than 20%. The overproduction theory and the nonutilization theory have been hitherto the two opposing explanations for the diabetic syndrome. The speaker measured the rate of utilization of sugar in the peripheral tissues and also the rate of sugar output by the liver. The rate of utilization was found to vary directly with the height of the blood sugar level in dogs subjected to pancreatectomy as in the normal dog. The diabetic dog utilizes less sugar than does the normal dog at every glycemic level. In order to utilize the same amounts of sugar, the blood sugar level of the dogs subjected to pancreatectomy must be about 200 mg. per 100 cc. higher than that of the normal dog. At the same blood sugar level the dog that has had pancreatectomy can utilize much less sugar than the normal dog.

With the use of liver catheterization and the bromsulphalein method for the estimation of hepatic blood flow, the absolute amounts of sugar entering and leaving the liver per unit time were calculated. The difference between them is the net rate of output of sugar from the liver. The rate of the output of sugar from 100 gm. of liver per minute was 14.5 mg. in normal dogs; 30.1 mg. in alloxan-diabetic dogs; 25.7 mg. in dogs in which partial pancreatectomy had been done (the remnant was 20%); and 34.5 mg. in the dogs in which total pancreatectomy had been done. In diabetic dogs (subjected to pancreatectomy) the output of sugar from the liver is increased and the utilization of sugar in the peripheral tissues is decreased. The average blood sugar level of normal dogs was 78 mg. per 100 cc.; that of the alloxan-diabetic dogs, 164 mg. per 100 cc.; and that of dogs subjected to pancreatectomy 148 mg. per 100 cc. The hepatic regulating mechanism for the control of blood sugar level does not respond to the change of the blood sugar level as rapidly and smoothly in dogs subjected to pancreatectomy as in normal dogs. In dogs subjected to pancreatectomy the breakdown of the protein and the formation of ketone bodies are greatly accelerated. The average basal insulin requirement of 10 dogs in which total pancreatectomy was done was 0.019 units per kg. of body weight per hour. This value if applied to a man weighing 60 kg. for 24 hours would equal 27 units, which agrees with the heretofore reported insulin requirement, i. e., 20 to 30 units in men in whom total pancreatectomy has been done. The basal insulin requirement of dogs in which partial pancreatectomy has been done (0.02 units) is less than that of alloxan-diabetic dogs (0.042 units), and that of the dogs subpected to total pancreatectomy (0.019 units) is slightly less than that of those subjected to partial pancreatectomy. This may be due to the existence of the hyperglycemic factor in the pancreas.

The three characteristics of pancreatic diabetes are: (1) the insulin requirement is small compared with that for severe spontaneous diabetes; (2) loss of weight, which cannot be controlled by insulin; and (3) development of fatty change in the liver.

Glucagon is said to be a polypeptide, therefore it may be digested with trypsin. In order to prevent the breakdown of the hormone by the action of pancreatic juice during extraction,

the speaker ligated the pancreatic ducts of dogs. Three months later he administered alloxan to the dogs in order to destroy the B cells of the islands of Langerhans. From such a pretreated pancreas the hyperglycemic factor, glucagon, was extracted. With the use of liver catheterization and the bromsulphalein method, a marked increase of output of sugar from the liver occurred soon after intravenous injection of glucagon, and consequently a steep rising of blood sugar level, resulting in the decrease of glycogen content of the liver, was seen. In the eviscerated dog the injection of glucagon did not cause any fluctuation of the blood sugar level. All these effects of glucagon are similar to the action of epinephrine. Glucagon has, however, no epinephrine-like actions on the cardiovascular system. It lowers the arterial blood pressure after a slight rise. In alloxan-diabetic dogs, whose B cells of the pancreas are completely destroyed, the blood sugar level is raised by vagus stimulation, so that glucagon is presumably secreted by vagus stimulation simultaneously with insulin. Glucagon increases the supply of blood sugar from the liver.

On the first day after pancreatectomy, the urine volume decreases. Thereafter the urine volume gradually increases and the water balance becomes negative. The volume of the extracellular fluid decreases, but the total body water decreases more rapidly, so that the intracellular fluid decreases and the animals lose weight. The osmotic concentration of the blood becomes elevated. The osmotic concentration of the urine does not decrease despite the markedly increased excretion of urine. Consequently the loss of electrolytes may be large. Serum sodium level decreases markedly, but the serum chloride does not decrease in proportion to the sodium because sodium has transferred into cells in place of potassium. The serum potassium level becomes gradually elevated.

All these disturbances of water, electrolytes, and acid-base equilibrium can be completely restored by insulin administration. When the plasma sugar rises above a certain concentration, the quantity of glucose presented to the renal tubules by the glomerular filtrate exceeds the reabsorption capacity. The sugar that thereby escapes reabsorption limits reabsorption of water in the terminal tubules. In addition, the glucose that accumulates in the extracellular fluid, being unable to penetrate cells freely, increases the effective osmotic pressure of this fluid. This draws water from the tissue cells and inhibits the reabsorption of sodium chloride through the tubules. The net result is polyuria, dehydration, and salt depletion.

The protein-bound iodine level decreases immediately after pancreatectomy as in the usual operation, but it rises progressively, exceeding the preoperative value. Histologically the thyroid gland shows evidence of hyperfunction. The excretion of 17-ketosteroids and the corticoid level of the serum increases, the eosinophil count decreases, and the 17-hydroxycorticoid level increases to about twice normal. Histological features of hyperactivity are seen 10 days after the operation in both the zona glomerulosa and the zona fasciculata. In general surgery the elevation of corticoid limits corticogenic hypothyroidism, but in pancreatectomy both the adrenal cortex and the thyroid become hyperactive. Follicular atresia and increase of the interstitium of the ovaries can be seen and estrogen decreases. After pancreatectomy special cells appear in the anterior and posterior lobe, intermedia, pars tuberalis, and eminentia medialis of the pituitary. The cells are most distinctive when stained by Nissle's method. They may be round, oval, or elongated. The outline is ragged. The nucleus contains gross chromatin granules and dense nuclear membrane and is darkly stained. The cytoplasm is thick or thin and is stained metachromatically a deep yellow-brown, so that the cells can be identified easily even by weak magnification.

The amount of diastase in the feces always decreases in one or two weeks after pancreatectomy, but it returns rapidly to normal in four or five weeks if not more than 20% of the gland is removed. The amount of trypsin in the feces is markedly decreased following pancreatic resection and shows insufficient recovery, even if the remnant is 20% of the original weight of the gland. The amount of lipase in the feces does not decrease following pancreatectomy.

NORWAY

Acute Poisoning.—Recent publications in the Scandinavian medical press concerning hospital admissions for acute poisoning show a strikingly uniform pattern. There has been a substantial rise in the number of such cases and a dramatic fall of their death rate. In the three medical departments of the Ullevål City Hospital there were 1,205 such admissions in the four year period from 1950 to 1953. This represented 5% of all admissions. In the *Journal of the Oslo City Hospitals* for March, 1955 (vol. 5, no. 3), Dr. Georg Omland points out that men outnumbered women (696 to 509), largely because of the great number of cases of acute alcoholic poisoning in men. Alcoholism was the chief factor in 464 cases. In most of these cases the alcoholism was chronic and had led to the abuse of other drugs such as barbiturates. Mental disorders came next on the list of etiological factors with 383 cases. Erotic complications (including matrimonial conflicts) came third on the list with 275 cases. Drug addiction came seventh on the list with 76 cases. About one-third of the cases were suicidal. At least 750 involved the use of barbiturates. A serum barbiturate level varying between 26 and 34 mg. per 100 cc. was found in the fatal cases. Most of those who recovered had a serum barbiturate level between 1 and 10 mg. per 100 cc. An important change in treatment was observed. In 1950 stimulants were given to 79 patients and in 1953 to only 5. On the other hand, efforts were made to keep the respiratory passages open in only 2 patients in 1950, while the corresponding figure for 1953 was 30. Oxygen was given to 20 patients in 1950 and to 60 in 1953. In the same period the number of patients receiving antibiotics rose from 37 to 110. The crude mortality rate of 5.8% is reduced to about 4% by omitting those patients who were brought in dead or dying. Omland pleads for the provision of a well-trained nursing staff qualified to put into force the measures recently shown to be beneficial. He also pleads for centralization of treatment and the provision of qualified psychiatric aid for this group of patients.

Tuberculosis Survey.—Dr. O. G. Hansen in *Tidsskrift for den norske lægeforening* for March 1, 1955, draws attention to the fact that the death rate from tuberculosis is declining much faster than the morbidity rate. In 1946 there were 1,665 deaths from pulmonary tuberculosis and in 1952 there were only 561. In the same years the number of new cases of infectious pulmonary tuberculosis reported fell from 3,833 to 2,325. During the period 1949 to 1951 mass radiography was carried out so effectively that about one million Norwegians over the age of 14 years were thus examined. About one in every 1,000 persons examined was found to have heretofore undetected infectious pulmonary tuberculosis. There were nearly twice as many men as women among these patients. It is difficult to disentangle the factors that may influence the behavior of tuberculosis. In 1947, when mass BCG vaccination was started, 29,630 such vaccinations were given. In 1952 this number had risen to 152,814. The fact that infectious pulmonary tuberculosis has diminished more effectively in the younger than in the older age groups suggests that BCG vaccine may be an important factor. Patients with intractable cavitation have become relatively rare in sanatoriums and so have the patients confined to bed. Many such patients have now been found to have disease amenable to chemotherapy, and the turnover of patients in sanatoriums is now much greater than it was, but the number of relapses has grown, readmissions now representing a large proportion of sanatorium clientele. Although chemotherapy often effects a cure, it does not prevent relapse.

Professional Secrecy for Physicians.—At a joint meeting in Oslo in February of a medical society and a legal society, attention was drawn to the anomalous state of affairs now existing in Norway with regard to professional secrecy for physicians, thanks to the pressure exerted by employers and health insurance authorities anxious to find out exactly what certain patients are suffering from. The Norwegian Medical Association has requested the government to appoint a committee charged with clarifying the whole problem. As matters now stand, the physician who wishes to fulfill all his obligations with regard to professional secrecy is likely to get into trouble whatever he does.

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CORRESPONDENCE

ORDERS FOR PATIENTS WITH ASTHMA

To the Editor:—I have just revised our standing orders for my asthmatic patients. We have 12 beds for asthmatic patients at Chicago Wesley Memorial Hospital, and we have been able to treat a large number of asthmatic patients in those rooms with very good results. Perhaps some of the readers of THE JOURNAL might be interested in these orders, since they might be of considerable help not only to the general practitioner but to the specialist.

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ORDERS FOR ADULT ASTHMATIC PATIENTS ON DR. UNGER'S SERVICE AT CHICAGO WESLEY MEMORIAL HOSPITAL

I. *Routine Entrance Orders*
1. Air filtered room, if possible.
2. Rubber pillows only (remove any feather pillows); rubber mattress preferred. *No smoking, no flowers.*
3. CBC, including differential.
4. Sedimentation rate (all cases), whether new or readmissions.
5. Kahn.
6. Urinalysis.
7. Sputum for both Tbc and eosinophiles.
8. ECG on all patients 40 or over (portable if much wheezing or receiving I.V. drip).
9. Fasting A-G ratio and sugar on all patients over 40 (delay if receiving I.V. drip).
10. Fasting blood cholesterol if anemia of unknown origin or suggestion of hyper- or hypothyroidism. In such cases BMR also, but delay if wheezing or if receiving epinephrine or ephedrine.
11. Quart fruit juice with 5 oz. glucose daily (unless diabetic).
12. Chest fluoroscopy and x-ray film (delay if receiving I.V. drip).
13. Benadryl, 25-50 mg. q.h.s. (more, if necessary), or 25 mg. Phenergan.
14. NO MORPHINE AT ANY TIME. Also avoid Demerol, Seconal, Nembutal, Amytal, codeine, etc. Whiskey and aspirin O.K. (unless contraindicated).
15. Inquire re allergy to drugs and note on outside of history holder (especially as re iodides, aspirin, penicillin, streptomycin).
16. Inquire re allergy to foods but only avoid those the patient is sure causes symptoms *(don't rely entirely on skin tests).*

II. *For Severe Cases*
1. Reassure patient. This is the most important therapeutic measure. Tell patient improvement will be rapid.
2. Start I.V. drip with 20 units liquid preparation ACTH (not gel) (unless ACTH contraindicated), plus 0.48 Gm. aminophylline (20 cc.), in liter 5% glucose in water. If patient gasping add epinephrine (adrenalin) 1.0 cc. 1:1000 dilution in first liter only; continue the ACTH and aminophylline in all subsequent liters. Try to average 3 liters per 24 hours for the severe cases. (For those who cannot be given ACTH merely give the aminophylline in glucose, with or without 1 cc. 1:1000 epinephrine.) When I.V. drip is stopped shift to ACTH-gel 40-40, 30-30, 20-20, 10-10 (twice daily), then stop if possible. If not, start one of the oral cortisone products.
3. Unless improvement is rapid inject 0.20 cc.-0.30 cc. Sus-Phrine (Brewer) subcutaneously morning and night (long-acting epinephrine).
4. If asthma is severe, may also give small amounts 1:1000 epinephrine subcutaneously p. r. n. (about 0.25-0.50 cc.).
5. Inhalations O_2 only for cyanosis.
6. Antibiotic therapy, e. g., some form of penicillin by injection, if evidence of infection (fever, leucocytosis, increased sedimentation rate, rales other than wheezing, or x-ray findings).
7. Apomorphine—KI prescription (unless allergy to KI).
   ℞ Apomorphine HCL gr. II (0.13 Gm.).
   Potassium iodide drams V (8.86 Gm.).
   Syr. cherry q.s.ad fl. oz. IV (120 cc.).
   Sig: One teaspoonful q.i.d.
8. Ephedrine may be added, if necessary, e. g., Searle's Amodrine or Lilly's Amesec.
9. Bronchoscopic aspirations may be life-saving in patients who are too weak to expectorate thick tenacious sputum.
10. Those receiving ACTH or Cortisone are to be on low salt diet and should also receive KCl. (0.50-1.0 Gm. t.i.d.).

III. *Milder Cases*
1. Epinephrine solution (1:1000), 0.20-0.40 cc. q. 4-12 hrs., if necessary.
2. Sus-Phrine (Brewer) 0.20-0.30 cc. subcutaneously, b.i.d., if necessary.
3. Aminophylline 10 cc. (0.24 Gm.; 3-¾ gr.) I.V. (use 10 cc. all glass eccentric syringe with 23-24 gauge needle),—take 4 to 5 minutes for this injection and repeat in 8-12 hours, if necessary.
4. Aminophylline rectally, either (a) 10 grains (0.67 Gm.) dissolved in 20 cc. tap water and instilled into rectum, especially at night; or (b) 7½ grains (0.50 Gm.) in a suppository.
5. Apomorphine—KI prescription, 1-4 times daily.
6. Glucose—fruit juices daily.

IV. *For Children*
1. Reassure.
2. Epinephrine (1:1000), 0.10 to 0.25 cc. subcutaneously and repeat q. 4-8 hours, if necessary.
3. Sus-Phrine (Brewer) 0.10 to 0.20 cc. subcutaneously once or twice daily, if necessary.
4. If asthma severe give 1 teaspoonful syrup Ipecac orally, and repeat once if child has not vomited within 60 minutes. (This frequently brings great relief.)
5. Rubber pillows, etc.

ROUNDS. Frequent rounds should be made. Make late check-up about 10 to 11 P. M. so that patient, interne and resident all sleep well. Any patient who is wheezing and is not receiving I.V. drip should then be given therapy, e. g., 10 cc. aminophylline I.V. Avoid strong sedatives as they are frequently harmful to patients with pulmonary diseases, including asthma. Whiskey (1-2 oz.) and 10 grains aspirin (unless allergy) make an excellent combination in most cases. Be cheerful.

CORTISONE AND IDIOPATHIC FACIAL PARALYSIS

To the Editor:—In THE JOURNAL of April 30, 1955, page 1599, Dr. Fred B. Moor of Los Angeles in an article, "Diagnosis and Treatment of Idiopathic Facial Paralysis (Bell's Palsy)," reviews the best accepted routine treatment for Bell's palsy. From the pathological standpoint he states that the cause is due to ischemia caused by pressure (edema). He did not mention an important recent medicament, cortisone, which appears to give excellent results in very early cases. The use of cortisone was brought to my attention by *Audio-Digest* of Feb. 19, 1954, in which an abstract was given of a case report published in THE JOURNAL of Jan. 9, 1954, page 142. On Dec. 24, 1954, I treated a 32-year-old woman with an acute (apparently idiopathic) case the fourth day after onset. Cortisone was given orally, beginning with 200 mg. daily, graduated down to 25 mg. in 14 days. The patient made almost a complete recovery by Jan. 7, 1955. No evidence of palsy was noted Feb. 10, 1955.

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ADENOIDECTOMY

To the Editor:—This is written in protest to the abstract of the article by E. E. Brown in the *Archives of Pediatrics.* The abstract appeared in the Dec. 11 issue on pages 1461 and 1462 of THE JOURNAL. Either the abstract is incorrect or Dr. Brown is woefully misinformed when he says, "deafness, recurring otitis media, and mastoiditis are rarely improved by adenoidectomy." This statement is scientifically inaccurate and betrays a vast ignorance of the fundamentals of otology. The statement should more accurately read, "deafness, recurring otitis media, and mastoiditis are usually improved by adenoidectomy."

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CONJUNCTIVAL PETECHIAE AFTER USE OF STOMACH TUBE

To the Editor:—Many conditions that cause venous congestion in and around the eye such as whooping cough, labor, compression of the thorax, constipation, straining at stool, and vomiting may produce conjunctival petechiae. To this list may be added the use of the stomach tube. In a series of 36 patients on whom an Ewald tube was passed, conjunctival petechiae developed in 20. The age of the patients varied from 19 to 64 years. Men and women were equally affected. The petechiae varied from the size of a pinpoint to that of a poppy seed. Most were located in the lower and/or upper cul-de-sac. Usually one or two speckles were present, but in some patients they were present in large numbers. The distribution is not always bi-

laterally symmetrical; one side may be spared and the other side affected. In two patients only the veins in the inner corner of the eye were enlarged. The enlargement in these patients disappeared shortly. It may be that in this drastic way hidden varices in the orbital section of the facial veins can be detected. After six or seven days the petechiae are no longer visible. They cause no ocular discomfort. Petechiae due to nonmechanical causes remain longer. During and after labor petechiae are seen in about 90% of mothers, but these disappear quickly. One might think that with the eyes closed, owing to the protective effect of the lid pressure, petechiae would not be so common. In a simple aspiration of the stomach, even with a large caliber tube, there is not enough time to produce the necessary damming back of blood. It may be that in some patients the petechiae represent little strokes.

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GOVERNMENT SERVICES

AIR FORCE

New Medical Insignia.—A new medical insignia design has been developed for use by Air Force Medical Service physicians and dentists in the near future. Flight surgeons will continue to wear their wing insignia. The new insignia is a small silver badge with a caduceus, or serpent, entwined on a staff and mounted in its center. The dental badge is identical to the one to be worn by physicians except for a "D" superimposed on the caduceus. The badge will be worn above the left breast pocket. The new insignia was developed by the heraldic section of the Air Force under the guidance of Brig. Gen. Otis O. Benson Jr., a flight surgeon with the Air Force Medical Service. The badge is not in production as yet. It will be several months before exact specifications are released to manufacturers.

Long-Distance Mercy Flight.—A plane took off from Brooks Air Force Base in Texas at 2 a. m. May 21, paused at Travis Field, Calif., and left there at 11:25 that night for Hickam Field, Hawaii. It was expected to make a stop at Guam on its way to the Philippines and to return by the same route after picking up a poliomyelitis patient, the wife of a serviceman and mother of three small children. Capt. Edward M. Miller of the school's department of radiobiology was the surgeon in charge of the Philippine flight. The aluminum lung, designed by physiologists at the School of Aviation Medicine for such emergencies, is a full-body shell of metal, similar to the massive types used in hospitals, but it weighs one-tenth as much. It operates on aircraft electrical systems as well as on standard house current, batteries, or hand bellows and can be carried aboard the plane or ambulance like a stretcher. In the past few months, aeromedical personnel from Military Air Transport Service and the air force school have flown with the respirator to Saudi Arabia, Tokyo, Germany, Puerto Rico, Alaska, and several times to Mexico City for poliomyelitis cases. The Philippine flight is the second to that Pacific island republic.

Personal.—Col. Edgar L. Olson, former surgeon of the Fifth Air Force in the Far East, has been awarded the Korean Military Merit Ulchi medal with Silver Star. The presentation was made at the School of Aviation Medicine, where he is now assigned as chief of clinical medicine. The citation, signed by Korea's Minister of National Defense, noted Colonel Olson's "remarkable interest and cooperation" in providing facilities to train surgeons for the Republic of Korea Air Force in the course of his Far East tour.

NAVY

The Smith Lecture.—Dr. Alan Gregg, vice-president of the Rockefeller Foundation, delivered the annual Harold Wellington Smith Lecture at the Naval Medical Center, Bethesda, Md., April 28. His lecture was entitled "On the Reading of Medical Literature."

Retirements.—Capt. Robert A. Bell was placed on the retired list of the Navy, May 1, after more than 23 years' service in the Medical Corps. Capt. Donald O. Wissinger was placed on the temporary retired list of the Navy, May 1, after more than 23 years' service with the Medical Corps. Capt. Harold Hirshland was placed on the retired list May 1, having reached the statutory retirement age. Captain Hirshland, however, will continue to serve at the naval station, Long Beach, Calif., on active duty until 1957.

VETERANS ADMINISTRATION

Personals.—Dr. Peter A. Volpe, manager of the 3,092-bed Veterans Administration hospital at Hines, Ill., resigned, effective May 1, and was succeeded in that position by Mr. Harry R. Pool, manager of the VA center in Fargo, N. D. Mr. Pool joined the veterans bureau in 1921 and has been manager also of the regional office in Minneapolis and of the VA hospital in Wilkes-Barre, Pa.——Dr. Howard P. Morgan, chief of professional services at the Veterans Administration Hospital, Roanoke, Va., has been appointed manager of the 781-bed neuropsychiatric VA hospital in Fort Lyon, Colo., succeeding Dr. Mansell B. Holmes, who resigned effective March 31, 1955.——Dr. Walter H. Buckholts, presently manager of the VA hospital at McKinney, Texas, in addition to his present duties also will assume the management of the VA hospital at Dallas.

Hospital News.—Dr. Arnold P. Friedman, physician-in-charge, Montefiore Hospital, New York, addressed the staff of the veterans administration hospital at Northport, N. Y., on May 20, on "Differential Diagnosis of Headache."

PUBLIC HEALTH SERVICE

Directory of Cancer Services.—"Cancer Services and Facilities in the United States, 1954," compiled by the National Cancer Institute, lists for the first time institutions and laboratories offering tissue diagnostic and cytodiagnostic services and homemaker services available to cancer patients. The directory gives names and locations of cancer hospitals and clinics and includes home medical care provided by hospitals and home-nursing services. It lists for each state the agency administering the official cancer program and the voluntary agency carrying on a statewide program. There are 17 cancer hospitals located in eight states and Puerto Rico, the directory reports, and nearly 800 visiting nurse associations throughout the country, from which cancer patients may obtain part-time home-nursing services. Hospitals in 14 states and the District of Columbia provide home medical care service. About 100 social agencies in 71 cities offer homemaker services, which in some cases are available to cancer patients. This directory can be purchased from the Superintendent of Documents, Government Printing Office, Washington 25, D. C., for 45 cents a copy.

Personals.—Dr. Ludwig von Sallmann, professor of ophthalmology, College of Physicians and Surgeons, Columbia University, will join the National Institute of Neurological Diseases and Blindness as visiting scientist on Aug. 1, to direct and expand its eye research program at the Clinical Center. Dr. von Sallmann will continue his studies there on ocular neurophysiology and ocular pharmacology and is now recruiting a research staff for these and other investigations.——Dr. Will H. Aufranc has been appointed regional medical programs consultant in the Department of Health, Education, and Welfare, Region IV, Atlanta, Ga., the U. S. Public Health Service announces. Prior to being commissioned in the Public Health Service in 1942, Dr. Aufranc served with the Missouri State Department of Public Health and Welfare.

LAW DEPARTMENT

MEDICOLEGAL ABSTRACTS

Charitable Hospitals: Liability to Paying Patient for Negligence of Servant.—The plaintiff sued the defendant hospital for damages on account of injuries allegedly caused by the negligence of its servants. From a judgment for the defendant, the plaintiff appealed to the Supreme Court of North Carolina.

The plaintiff, an infant, alleged that she was admitted to the defendant hospital to be treated for pneumonia; that she suffered third degree burns while under a "croup tent," which burns were caused by the negligent acts of the defendant's employees; and that her father paid for all of the services rendered to her while in the hospital. The defendant alleged that it was a charitable institution, but the plaintiff moved to dismiss this answer as being irrelevant to her right to recover. It contended that the court should either overrule its prior rulings that charitable institutions are immune from suits or hold that the plaintiff's suit was not barred by the immunity rule because she was a paying patient.

The Supreme Court stated that the immunity rule set forth in earlier decisions is that a charitable institution is not chargeable with the negligence of its employees committed while rendering charitable services, unless it is shown that the charity has been careless in selecting and retaining incompetent employees. In the opinion of the Court, the majority of jurisdictions still apply some type of immunity rule to charitable institutions. Since the immunity rule is well established in the state, said the Court, the policy of stability in the law is of more significance than any of the plaintiff's reasons for making the proposed change. Whether or not a change is advisable is a question of broad public policy. It should be resolved by the law-making body, not by judicial legislation. The Court also concluded that a charitable institution, when rendering services consistent with its purposes, is deemed to be rendering charitable services, even though the particular recipient paid a reasonable fee therefor. In other words the fact that a patient paid for the services rendered does not affect the immunity rule.

Accordingly, the court affirmed the judgment in favor of the defendant hospital. *Williams v. Randolph Hospital, 75 S. E. (2d) 303 (N. C., 1953).*

Malpractice: Electroshock Treatments; Application of Res Ipsa Loquitur.—The plaintiff, by a guardian *ad litem,* sued for damages resulting from injuries received during the alleged negligent administration of an electroshock treatment. From a judgment in favor of the defendants, the plaintiff appealed to the Supreme Court of California.

In 1936, at the age of 19, the plaintiff became mentally ill, suffering from chronic schizophrenia with hebephrenic and paranoid features. The plaintiff was privately cared for by his father until 1944, when he was committed to Camarillo State Hospital. In 1947 the plaintiff was paroled from Camarillo on the condition that his father would be responsible for his care; the parole also provided that the father could place the plaintiff in the Los Angeles Neurological Institute, a licensed private psychiatric institution. While under his father's care and supervision, but not at the institute, the plaintiff underwent a lobotomy operation on June 27, 1948. On Aug. 29, 1948, the father placed the plaintiff in the institute. While there, the defendant, one of the directors of the institute, agreed, at the suggestion of the father, to give the plaintiff electroshock treatments. The plaintiff had been given some 80 such treatments before. The father signed a written consent to the treatment. At this time the plaintiff's condition was considerably worse than before.

On Aug. 30, 1948, the defendant gave the first of such treatments to be given. On Sept. 1, 1948, another was given. A few seconds after the current was applied, and while the plaintiff was still in a state of convulsion, the defendant and the attending nurses heard a snapping or crunching sound. Subsequent x-rays revealed that both of the plaintiff's femur bones were broken close to their heads.

The plaintiff sought to recover on two theories: (1) that the administration of shock therapy treatments constituted batteries since he had not personally consented thereto and (2) that the broken femur bones resulted from the negligence of the defendant. The evidence indicated that fractures occur as a result of muscle tension, that a high degree of muscle tension results from an electrical shock treatment, causing convulsion, and that, as a consequence, fractures in any part of the body are an inherent risk of shock therapy, no matter how well or carefully it is administered. The evidence also disclosed a conflict as to how many attendants should be present to restrain the patient during the period of convulsion, some experts believing the least degree of restraint to be the best practice, and some believing a great degree of restraint to be the best practice. Apparently, the defendant had either two or three nurses helping him.

The Supreme Court held that the defendant was not guilty of a battery, even though the plaintiff was an incompetent adult for whom at that time no court had appointed a guardian. The Supreme Court based its decision on the fact that the plaintiff had been an inmate at Camarillo (a state institution) at one time and had been lawfully released to his father under a parole that authorized his father to do such things in the care of the plaintiff as consent to shock treatments. In other words, while a court-appointed guardian did not consent to the treatment, still, it was done in pursuance of the laws of California.

The Supreme Court also reached a decision favorable to the defendants on the issue of negligence. The plaintiff argued that the jury should have been permitted to decide whether the defendant had acted negligently, since the doctrine of *res ipsa loquitur* applied. The Supreme Court held that the doctrine applies in malpractice cases only where the jury, as laymen, could infer from the facts that the injury complained of ordinarily would not have happened unless the defendant doctor had in some way acted negligently. In the instant case the injury was the ordinary, or at least the probable, consequence of shock treatment, regardless of the carefulness involved. The mere fact that it happened was not in and of itself indicative of negligence.

Accordingly, the Supreme Court affirmed the judgment in favor of the defendant physician. *Farber v. Olkon, 254 P. (2d) 520 (Cal., 1953).*

Zoning Restrictions: Variance Allowed for Physician's Office.—The plaintiffs filed suit to contest an action of the New Haven Board of Zoning Appeals granting a zoning variance to the defendants. From a judgment sustaining the action of the board, the plaintiffs appealed to the Supreme Court of Errors of Connecticut.

The defendants, having purchased a 13 room residence located in an area zoned for residential use, including boarding houses and hotels, applied for a variance that would permit them to use the building for offices for physicians and dentists. The variance was granted on grounds that the house was too large to be suitable for residential purposes under modern conditions and that conversion to a medical office building would be more beneficial to the community than the establishment of a boarding house. It appeared furthermore, that many other buildings in the vicinity were also being used by physicians and dentists and that the neighborhood was becoming a medical center.

The Supreme Court of Errors held that the board properly granted the variance. The validity of zoning variances, said the court, is tested by their effect upon the comprehensive plan of the municipality. The court was of the opinion that the board had reasonable grounds for holding that the granting of this variance did not adversely affect the over-all plan in view of the changing character of the community. It could not therefore be said that the board acted "arbitrarily, illegally or so unreasonably as to have abused its discretion."

The judgment in favor of defendants and approving use of the property for doctor's offices was accordingly affirmed. *Parsons v. Board of Zoning Appeals, 99 A. (2d) 149 (Conn., 1953).*

MEDICAL FILM REVIEWS

Antituberculosis Drugs in the Medical and Surgical Treatment of Tuberculosis: 16 mm., color, sound, showing time 30 minutes. Prepared by H. Corwin Hinshaw, M.D., Stanford University School of Medicine. Produced in 1953 by Billy Burke Productions, Hollywood, for and procurable on loan from E. R. Squibb & Sons, 745 Fifth Ave., New York 22.

This pictorial clinic indicates the expectable benefits as well as the limitations of such antituberculosis drugs as *p*-aminosalicylic acid (PAS), streptomycin, dihydrostreptomycin, and isoniazid (Nydrazid). It is made up of patients from 7 weeks to 74 years of age with the disease in every stage from the earliest to the most advanced. It shows that modern drug therapy can be expected to give maximum benefit, even complete remission, through early prescription, and it also shows the type of benefits expectable from drug therapy applied in cases that are more progressed. The role of drugs in localizing the disease, preparatory to definitive surgery, is discussed in detail. This is a comprehensive picture of the modern sanitarium and drug and surgical treatment of pulmonary tuberculosis. By stressing the continuing importance of bed rest and sanitarium care and by showing the complexities concerned in the treatment of every individual case, it should do much to discourage the home treatment of tuberculosis by physicians inexperienced with the disease who have an overhopeful belief that the new drugs are all that is required. As a production, this film is very well done, and the photography and narration are excellent. It should be of great interest to all persons concerned with tuberculosis problems, including lay workers, nurses, general practitioners, and those specializing in the medical and surgical management of the disease.

Intravenous Anesthesia with Barbiturates: 16 mm., color, sound, showing time 33 minutes. Produced in 1953 by Mervin LaRue, Inc., Chicago, for Abbott Laboratories under the joint sponsorship of the American College of Surgeons and the American Society of Anesthesiologists, Inc. Procurable on loan from Abbott Laboratories, North Chicago, Ill.

This is a step-by-step record of the intravenous administration of barbiturate anesthesia in a clinical case. It includes information on the characteristics of intravenous barbiturate anesthesia, the chemical structure, the principal actions and effects of thiobarbiturates, the factors determining what premedication shall be given, and the advantages of atropine or scopolamine, barbiturates, and opiates. Fitting each induction to the needs of the patient and the surgeons, patient tolerance, rate of injection, and obtaining maximum muscle relaxation by complementing barbiturate anesthesia are also discussed. Protecting the air passage throughout the period of unconsciousness, assisting the depressed respiratory function, and handling laryngeal or pharyngeal reflexes if they should occur are mentioned. The principles and statements brought out in this film are correct, and they need to be emphasized. Some of the effort to illustrate a resident in training in anesthesiology gives one the impression from the doctor's unsmiling face that he feels an evident regret that he must lecture to medical students, and this, in turn, gives the impression that anesthesiology is work for him rather than pleasure. It may also leave the impression that the man in charge has left the hospital and that the resident has no one to turn to if he should get into trouble. Actually this impression should not be gained, since it is made clear that the resident is well trained and competent to do the job. The film could be improved by eliminating the introduction and beginning with the chemical formulas. The film might well be terminated when the individual who administered the anesthetic makes his brief postoperative call on the patient and before the attending doctor appears on the scene. Nevertheless, it has so many merits that it should be shown to as many groups as possible. Those who have the least knowledge of anesthesia will be the least critical of it, but, in any event, no one can deny that the message itself is correct. The photography is done beautifully, and the film is about the right length for use at a lecture or medical meeting.

Health: Your Cleanliness: 16 mm., black and white, sound, showing time 11 minutes. Technical Supervisor: Dr. Dorothy B. Nyswander. University of California School of Public Health. Produced in 1953 by Centron Corporation, Lawrence, Kan., for and procurable on purchase ($50) from Young America Films, 18 E. 41st St., New York 17.

This film discusses the importance of cleanliness in health and sickness and the general health rules regarding such things as bathing, care of nails and hair, clean clothing, and teeth. It portrays for intermediate grade school students the desirability of personal cleanliness and the ways it can be obtained. Mention is made of such cleanliness factors as bathing and washing of the hands and face, with particular emphasis on washing the hands before eating, before associating with other people, and after using the toilet. Teeth brushing and the reasons for it are completely presented; the need for clean clothing, with special emphasis on underclothing, is also presented. Cleanliness and care of the hair and fingernails are emphasized. The relationship of personal cleanliness to other activities is pointed out in pictures of the operating room, of the sickroom, of the playground, and of other activities of daily living. Although it is not stated that acne is caused by the accumulation of dirt, this is implied strongly, and the statement "the accumulation of dirt on the skin blocks the pores" is not true. Cleaning fluid should not be used by children of these ages, as it might prove dangerous. Although this film is directed toward the fourth, fifth, and sixth grades, the material will not be accepted by children of these ages. It is definitely a supplement to other basic teaching.

Travert—Electrolyte Highlights—The Role of the Ion: 16 mm., color, sound, showing time 18 minutes. Produced in 1954 by Mervin LaRue, Inc., Chicago, with the technical assistance of William E. Abbott, M.D., Cleveland, and Harry F. Weisberg, M.D., Chicago. Procurable on loan from Baxter Laboratories, Inc., 6301 Lincoln Ave., Morton Grove, Ill.

This film familiarizes the audience with the composition of 10 solutions of different electrolyte content prepared by the sponsor. Indications for the use of each of these solutions in selected cases of electrolyte deficiencies are presented. A well-animated pictorial presentation of the fluid compartments of the body, of their ionic composition, of interchange of ions, and of metabolic acidosis and alkalosis suffers from oversimplification. The time allotted to a presentation of electrolyte balance is inadequate. The attempt to crowd into the film a pathophysiological consideration of deficiencies in individual ions such as sodium, potassium, chloride, calcium, magnesium, and phosphate further diminishes the educational potential of the picture, since too many important facts and considerations for the indication of these fluid preparations have been omitted. The use of the term Travert for invert sugar may be confusing to some physicians. At least somewhere in the presentation it should be made clear that Travert is invert sugar. In view of the inadequacy of its content, the picture cannot be recommended to medical students and practitioners.

The Recurrent Laryngeal Nerve in Thyroid Surgery. A Triangle for Its Localization and Protection: 16 mm., color, silent, showing time 15 minutes. Prepared in 1948 by and procurable on rental ($5) from M. M. Simon, M.D., 96 Hooker Ave., Poughkeepsie, N. Y.

This film depicts an anatomic triangle bounded by the recurrent laryngeal nerve, the inferior thyroid artery, and the common carotid artery. The film presents the view that identification of this triangle protects the recurrent laryngeal nerve and avoids injury to it in the course of thyroid surgery. Such a triangle is a useful adjunct in surgical anatomy. Simon has dissected 43 cadavers, or a total of 86 triangles, and demonstrates statistically the relationship between the recurrent laryngeal nerve and the inferior thyroid artery. Although neurovascular anomalies are encountered, the triangle remains constant. Some anatomists might object to the term "extracapsular" in the identification of many structures. Some surgeons and anatomists believe that a surgical capsule is nonexistent. This fact in no way detracts from the value of the triangles herein demonstrated. The film would be far more impressive if, after the demonstration, the structures were presented on a living patient in the course of a thyroidectomy. This film can be recommended for medical students and those interested in surgical anatomy.

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MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Pernicious Anemia: Evaluation of Its Diagnostic Features. M. P. Neal. South. M. J. **48:**238-244 (March) 1955 [Birmingham, Ala.].

The diagnosis of untreated pernicious anemia is usually not difficult to make if the diagnostic symptoms, signs, and simple laboratory procedures are interpreted correctly. The difficult cases are those in which these diagnostic features have been destroyed by "shotgun" treatment for anemia before its proper classification. Clinically, pernicious anemia is characterized by a slow insidious onset, yellowish pallor, languor, slowly developing weakness, faintness, sore tongue, digestive disturbances, numbness and tingling of hands and feet, paresthesias, palpitation, dyspnea on exertion, and often spastic paresis with decreased deep sensitivity. From the laboratory standpoint, the disease is a macrocytic anemia with megaloblasts, ovalocytes, a color and volume index above normal, a high mean corpuscular hemoglobin value, hypersegmented neutrophilic leukocytes, and an absence of free hydrochloric acid in the gastric juice. The author has drawn up a diagnostic chart in which 12 features of pernicious anemia are grouped together, each counted as 8.33% of a typical case of the disease. These factors are: (1) the chronic idiopathic remittent nature of the illness with a progressive malignant course; (2) glossitis and digestive disturbances with achlorhydria; (3) posterior lateral sclerosis with disturbed locomotion and paresthesias; (4) erythrocytopenia, often to 2 million or less per cubic millimeter; (5) abnormality of red cells with regard to size, nucleation, and staining properties; (6) reticulocytosis at the onset of remissions; (7) blood color index and volume index each above 1.0; (8) leukopenia with slight lymphocytosis; (9) hypersegmentation of neutrophils, giving a nuclear shift to the right; (10) hypoproteinemia; (11) subclinical jaundice, with an icterus index of 7 to 20; and (12) favorable response to anti-pernicious-anemia principle. A procedure developed by Segal, Miller, and Morton ascertains the absence or presence of free hydrochloric acid in the stomach through the use of an ion-exchange resin and without gastric intubation. The test is made on urine samples collected after a quinine resin preparation has been given orally. In the presence of free hydrochloric acid in gastric juice, measurable amounts of quinine are eliminated in the urine during a two-hour test period. Quinine is not eliminated in the presence of gastric anacidity. This method appears to be highly promising.

Familial Congenital Methemoglobinemia: Clinical and Therapeutic Findings. T. Chiaroni and F. Bonati. Minerva med. **45:**53-61 (Jan. 13) 1955 (In Italian) [Turin, Italy].

Familial congenital methemoglobinemia was found in two sisters, 18 and 13 years old, who were admitted to the cardiosurgical clinic of the University of Turin with a diagnosis of congenital heart disease. Although signs of definite heart impairment had not been present in these patients, the diagnosis was suggested by the fact that cyanosis had been present in both since their birth. The presence of methemoglobin in the blood of both patients was ascertained by spectrophotometric studies. Methemoglobin was not found in the blood of the parents and a brother of the patients, nor had the four grandparents (all dead) presented symptoms ascribable to methemoglobinemia. This agrees with the hypothesis that the condition may be transmitted as a recessive characteristic. The patients, who were followed for more than two years, were treated with methylene blue, ascorbic acid, and cytochrome C, and they were benefited. According to these authors, methylene blue should be used for toxic methemoglobinemias that are so pronounced as to endanger severely the functions of the organism. Ascorbic acid, in the diet as well as in the form of a drug, should be used for idiopathic congenital forms of the condition. The less prompt and less complete action of this vitamin with respect to that of methylene blue is greatly compensated by the advantage that with the vitamin a "physiological" substance is introduced into the body that is usually present in food and in intraorganic humors. It can also be administered in therapeutic doses for an indefinite period without harmful effects to the patients. The fact that the blood of these two sisters belonged to different groups indicated that methemoglobinemia is independent of the blood group character.

Some Clinical Observations of Asbestosis in Mine and Mill Workers. P. Cartier. A. M. A. Arch. Ind. Health **11:**204-207 (March) 1955 [Chicago].

Of 128 cases of asbestosis detected in mine workers between 1945 and 1953, 72 were cases of minimal, 35 of moderate, and 21 of advanced asbestosis. Forty patients died and autopsies were performed, while 88 patients are still living. Of the 128 patients, 62 were between the ages of 35 and 59, 50 were between the ages of 60 and 70, and 16 were over 70 years of age. Of the 40 patients who died, 6 obviously died of asbestosis, while in the other 34, lesions of cardiovascular disease, evolutive tuberculosis, and bronchial carcinoma developed that could well be considered as the cause of death, although the part played by the asbestotic fibrosis is not known. Of the 88 living patients, 59 are able to work without discomfort and in 40 with minimal or moderate asbestosis the clinical status is good. For the remaining 29 patients no good correlation between the degree of asbestosis and the clinical status has been found. Clinical data, such as cough, expectoration, and weight, cannot prove too much. The author believes that asbestosis is a serious disease in some instances, but more frequently it remains a disease that can be tolerated well for many years, even without appreciable symptoms, as long as another serious disease does not supervene. The combined effort of pathologists, physiopathologists, roentgenologists, cardiologists, and clinicians is needed to orientate any research program and to bring answers to the many unknown aspects of asbestosis.

Hepatic Coma, a Review of 27 Cases. C. Andrews, M. Delp and M. J. Elliott. J. Kansas M. Soc. **56:**125-129 (March) 1955 [Topeka, Kan.].

At the University of Kansas Medical Center all the charts carrying the diagnosis of hepatic or biliary disease during the years 1947 to 1954 were reviewed in order to find cases of hepatic coma. The following criteria established the diagnosis of hepatic coma: (1) the presence of coma associated with delirium, flapping tremor, fetor hepaticus, or other signs and symptoms usually associated with hepatic coma; (2) the presence of primary or secondary liver disease; and (3) the absence of any other disease that would adequately explain the coma. A total of 27 cases were found, and these are analyzed. The underlying liver disease was established by postmortem examination in 21 cases, by biopsy in 2, and on other evidence in the remaining 4. Diffuse hepatic fibrosis existed in 16, postnecrotic cirrhosis in 3, infectious hepatitis with massive hepatic necrosis in 3, biliary cirrhosis in 3, homologous serum hepatitis in one, and replacement of liver by tumor in one case. A factor likely to precipitate hepatic coma could be established in 10 patients.

The place of publication of the periodicals appears in brackets preceding each abstract.

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Ammonia-containing compounds were suspected in six, barbiturates or opiates in two, and paracentesis in one. Sixteen patients had evidence of gastrointestinal bleeding that was undoubtedly a factor in producing further hepatic insufficiency and coma. In commenting on ammonia-containing compounds as a precipitating factor in hepatic coma, the authors say that the administration of ammonium chloride led to hepatic coma in three patients. The condition of another patient, in whom a portacaval anastomosis had been established, was relatively good until an amino acid preparation was administered intravenously. After that, hepatic coma developed and he died. In another patient two episodes of coma were caused by the administration of an exchange resin. The course of a patient with diffuse hepatic fibrosis and ascites was uneventful until he received acetozoleamide (Diamox) as a diuretic; this was followed by the development of hepatic coma, from which he died. The authors observed two other patients with cirrhosis who became confused and lethargic but did not develop true coma after receiving this drug. Acetozoleamide (Diamox) blocks carbonic anhydrase in the kidney, and hydrogen ions necessary for the conversion of ammonia to the ionic form are not produced.

Unusual Manifestations of Rheumatoid Nodules: Report of Three Cases. W. M. Mikkelsen, I. F. Duff and W. D. Robinson. J. Michigan M. Soc. **54**:292-297 (March) 1955 [St. Paul].

Three patients with rheumatoid arthritis are described in whom rheumatoid nodules presented rather unusual features. In the first of these, tendon involvement with spontaneous rupture of the right extensor pollicis longus tendon appeared as the initial manifestation of the disease. Histological examination of material obtained during surgical repair of a subsequently ruptured tendon revealed a typical rheumatoid nodule at the rupture site. Steroid therapy was instituted in this patient in the hope of minimizing nodule formation and avoiding further tendon ruptures. The second patient was observed during her brief terminal course, which followed withdrawal of cortisone therapy. Postmortem examination revealed rheumatoid nodules in the subcutaneous tissues, lung parenchyma, splenic capsule, annulus fibrosus near the base of the aortic valves, pericardium, sclera, in one of the ciliary nerves, in extraocular muscle, and in the dura. The occurrence of typical rheumatoid nodules in the dura had not been reported previously, to the authors' knowledge. Because of persistent and progressive hoarseness the third patient was examined in an otolaryngology clinic, where lesions thought to be atypical "speaker's nodes" were observed on each vocal cord. Microscopic examination of material removed surgically from the right vocal cord revealed rheumatoid nodules remarkably similar in appearance to a previously removed subcutaneous nodule; this also seems to be the first case of its kind to be reported. The occurrence of persistent hoarseness in a patient with rheumatoid nodules and subcutaneous nodules should suggest the possibility of rheumatoid nodules in the larynx.

Diagnostic Problem of Spontaneous Subarachnoid Hemorrhage. F. Di Lollo and G. Truci. Sett. med. **42**:660-666 (Dec. 31) 1954 (In Italian) [Florence, Italy].

The diagnosis of spontaneous subarachnoid hemorrhage is reviewed on the basis of 90 patients with this condition who were seen by the authors from 1946 to 1954. The course of this condition can be divided into three stages, each of which is characterized by particular clinical findings. The initial period, which lasts from 6 to 12 hours, is characterized by the abrupt onset of headache, vomiting, and a temporary unconsciousness. Sometimes the last-named can appear without the first two signs and thus suggest the presence of a stroke owing to cerebral hemorrhage. This diagnosis can, however, be ruled out if the unconsciousness is substituted within a few hours and sometimes a few minutes by a phase of mental confusion, the length of which varies. As a rule, if the unconsciousness continues without remission for 24 hours, the diagnosis of spontaneous subarachnoid hemorrhage should be excluded, and the prognosis becomes unfavorable. The second phase is generally the period in which the patient is hospitalized. It lasts for an average of 15 days, and it is characterized mainly by signs of meningeal involvement, with a stiff neck, Lasègue's sign, and high, remittent fever. Most deaths of patients with this condition occur during this stage. The third or sequelae period is often missing, either because the patient died during the previous phase or else because his recovery was without sequelae. When it is present, this period is characterized by a headache that may be either continuous or occur in attacks, or by manifestations in foci. The distinction of the course of this condition into three phases is extremely useful from the clinical standpoint, especially because it simplifies the problem of differential diagnosis. This is discussed with regard to such intracranial alterations as cerebral hemorrhage, cerebral thrombosis, spontaneous cerebral hematoma, hemorrhagic meningoencephalitis, acute cerebromeningeal edema in hypertensive persons, cerebral tumors, and meningitis. It is also discussed with regard to conditions owing to extracerebral causes such as myocardial infarct and nervous symptoms.

Acquired Toxoplasmosis: With Report of a Case of Laboratory Infection. J. K. A. Beverly, E. Skipper and S. C. Marshall. Brit. M. J. **1**:577-578 (March 5) 1955 [London, England].

A case of toxoplasmosis resulting from a finger-prick sustained in the laboratory is described. The patient, one of the authors, had been filling a syringe with mouse peritoneal exudate rich in the Rh strain of Toxoplasma. After an incubation of nine days a mild illness characterized by fever and lymphadenopathy occurred. The diagnosis was made by means of the dye test, which rose to a high titer (maximum 1:4,200), but the organism could not be recovered by animal passage. Six other published cases of laboratory Toxoplasma infections were found in the literature. The clinical features of these cases vary but closely resemble those of the spontaneously acquired disease. One case resulted in death. A large number of compounds have been tried without success in the treatment of experimental toxoplasmosis in animals. So far, none of these drugs has been used in the treatment of human infections on a scale large enough to warrant drawing any conclusions. The laboratory worker whose case is presented here was treated for two days with penicillin without any effect on his pyrexia; it was not possible to ascertain whether or not there was a response to sulfadimidine.

Joint Fluid Changes in Rheumatoid Arthritis. W. D. Robinson, I. F. Duff and E. M. Smith. J. Michigan M. Soc. **54**:270-291 (March) 1955 [St. Paul].

The abnormal characteristics of the synovial fluid in rheumatoid arthritis were found to revert toward a more normal pattern under the influence of adrenal cortical steroids. With systemic therapy, by adrenocortical stimulation or oral or intramuscular administration of cortisone or hydrocortisone, these effects were most pronounced at high dosage levels. Following intra-articularly administered cortisone, these effects were not obtained consistently and lasted only a few days. Following intra-articularly administered hydrocortisone, such effects were more consistently obtained with small doses and were better sustained. It appears that this effect of the steroids is exerted on the synovial membrane and may account, at least in part, for the favorable clinical effect of these agents in rheumatoid arthritis. In addition to a decrease in polymorphonuclear cells, this reversion toward normal includes an increase in joint fluid viscosity attributable to an improvement in the physical chemical properties of the polysaccharide characteristic of synovial fluid, hyaluronic acid. Such changes indicate an effect of the steroids on connective tissue cells, where hyaluronic acid is presumably formed. These studies do not indicate whether the effect of the steroids at the connective tissue level is direct or secondary to suppression of inflammation. Certain conclusions appear justified concerning the clinical usefulness of long-term therapy with hydrocortisone acetate given intra-articularly in rheumatoid arthritis. The procedure is not suitable as a single form of treatment for this disease; it must be combined with other accepted forms of therapy. When this was done in selected patients with one or two joints that were refractory to other forms of treatment, intra-articular injections of hydrocortisone were associated with sustained, worth-while benefit in half of the joints treated. When combined with special orthopedic and

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physical therapy measures, this procedure proved a definite asset in the rehabilitation of selected persons. In some joints worthwhile symptomatic and objective relief was eventually achieved for a period of four to six weeks before repeat injections were required. On discontinuing therapy, symptomatic benefit persisted for from 4 to 18 months in 19% of all treated joints. In the remaining instances the injections were eventually discontinued because of lack of benefit or inadequate response. Seven detailed case reports are given.

The Palliation and Remission of Cancer with Combined Corticosteroid and Nitrogen Mustard Therapy: Report of 100 Cases. W. D. McCarthy. New England J. Med. **252**:467-476 (March 24) 1955 [Boston].

In an effort to develop a new approach to the definitive palliation of patients with advanced cancer, 100 such patients were treated with large doses of corticotropin or cortisone administered simultaneously with nitrogen mustard. The majority of the 100 patients were in advanced or terminal phases of cancer and had failed to respond successfully to previous surgical, radiation, or hormone therapy. Unusual temporary remissions for intervals as long as three years were obtained in 16% of patients, often with associated tumor regression or arrest. An additional 15% received good palliation with prolongation of life in increased comfort. The remaining 69 patients were classed as fair (29%) or poor (40%) in palliative response and received little or no benefit. It was particularly noteworthy that prolongation of life resulted only in patients who obtained definite palliation of symptoms. The corticotropin and cortisone successfully acted to abolish or greatly to reduce the severe nausea, vomiting, and bone-marrow depression usually caused by nitrogen mustard. Complications and side-effects were few and temporary. There is evidence that use of the method in earlier phases of cancer, its concurrent employment with radiation and triethylene melamine, as well as recent refinements in technique, will produce palliation and remissions superior to those reported in the present series. Case reports of 17 patients who had unusual subjective and objective remissions are described.

Histoplasmosis: Review with Epidemiological and Clinical Study of an Outbreak Occurring in Minnesota. R. T. Smith. Journal-Lancet **75**:83-100 (March) 1955 [Minneapolis].

The literature pertaining to histoplasmosis as a historic curiosity, as a clinical and laboratory entity, as a cause of nontuberculous pulmonary calcification, and as an epidemic pulmonary disease is reviewed. The view that histoplasmosis was a rare, fatal, disseminated fungus infection was widely held and universally taught until 1945. Between 1945 and 1950 this idea underwent complete revision, resulting in the concept that histoplasmosis is a common, benign infection occurring in most parts of the central United States. With increased appreciation of this fungus disease, clinical and epidemiological studies have revealed several clinical forms of infection not previously recognized. An epidemic outbreak of histoplasmosis in a Wright County, Minnesota, farm family is described. It involved at least eight members, whose illness ranged from a very mild pulmonary type to the fatal disseminated type of the disease. A probable source of infectious spores was demonstrated on the farm occupied by the affected family, but attempts to isolate the fungus were unsuccessful. A survey to determine the prevalence of skin sensitivity to histoplasmin and tuberculin in Wright County revealed an unexpectedly high incidence of reactors to histoplasmin in the southeastern corner of the county. A higher incidence of sensitivity was found in rural dwellers than in urban dwellers. Data were presented to indicate that a higher incidence of reactors was found in some families than might be expected by chance alone. Chest x-ray survey of all reactors revealed an incidence of calcification of about 25%, regardless of age. In the clinical spectrum of human histoplasmosis, seven distinct forms of the disease can be differentiated: disseminated, acute pulmonary, chronic pulmonary, and chronic local, all of which are clinically symptomatic; and a pulmonary form that may result in calcification, a form that manifests itself as an influenza-like illness, and a form that is translated by a positive skin reaction. The last three are clinically mild or asymptomatic. The author predicts that, with further research, new forms of the disease will be found and that, when the index of suspicion is raised in cases of unexplained pneumonitis, the incidence of histoplasmosis in Minnesota will be found to be greater than previously held.

SURGERY

Small Cell Carcinoma of the Thyroid Gland of Youth. J. A. Buckwalter and L. K. Meredith. Pediatrics **15**:317-321 (March) 1955 [Springfield, Ill.].

The occurrence of small cell carcinoma of the thyroid is reported in an 8-year-old boy. There was slow progressive enlargement of the child's neck. Four months before the patient's admission to the hospital there was a definite acceleration in the rate of growth of the mass. For one month there was a dry, hacking, nonproductive cough associated with wheezing respiration that was most severe in the recumbent position. Surgical exploration showed that the enlarged thyroid was invaded by a neoplasm that extended into the adjacent soft tissue. Total thyroidectomy was carried out, but residual tumor tissue remained on both sides of the neck. Tracheostomy was performed at the time of the operation. Postoperatively a total dose of 3,000 r was given through two ports, with no suggestion of a favorable response. Despite surgical and irradiation treatment there was rapid progress of the lesion. Indirect laryngoscopy showed paralysis of the left vocal cord. Examination of bone marrow revealed a substantial decrease in the normal elements and invasion and replacement of the marrow by clumps and masses of anaplastic neoplastic cells that tended to form epithelial bridges. Widening of the superior mediastinum was shown roentgenographically and was interpreted as extension of the tumor into this area. Death occurred after a massive hemorrhage from the tracheostomy seven months after enlargement of the neck had first been noted. The most striking feature was the rapid progress of the lesion, resulting in early death after ineffective partial surgical excision and external irradiation. The tumor did not take up radioactive iodine. The three fatal cases previously reported had much the same course. Surgery should be done early and an attempt made to extirpate all the gross neoplasm. Maximal doses of external irradiation should be used to supplement surgical extirpation, which by itself was in no instance judged to be adequate therapy.

Resection of the Aortic Bifurcation for Relief of a Mycotic Aneurysm of the Left Common Iliac Artery, and Its Replacement by a Preserved Arterial Graft: With a Discussion of the Treatment of Aneurysms, Illustrated by Three Further Examples. H. D. Moore and M. Telling. Brit. J. Surg. **42**:420 426 (Jan.) 1955 [Bristol, England].

The first part of this report is concerned with the history of a young woman in whom a mycotic aneurysm was discovered some months after she had been discharged as well, following treatment for bacterial endocarditis with massive doses of penicillin. Aortography revealed that the aneurysm arose from the left common iliac artery at its origin from the aorta. It was also beginning to erode the fourth and fifth lumbar vertebrae. Operation was considered essential. The resection and grafting of the aortic bifurcation for a mycotic aneurysm of the left common iliac artery is described. The graft used was arterial and had been stored in "Gross's balanced salt solution" at 1 to 8 C. Such operations are justified because of the poor prognosis in patients with aneurysms. The average survival of a patient with an aneurysm is about 18 months; but with a mycotic aneurysm the outlook is probably worse. Too few examples have been described since the introduction of antibiotics to be certain about this point. The aneurysms will disappear spontaneously in some patients, and some will live for many years, but no definite prognosis is possible in the individual case. No surgeon, apart from warfare, is likely to see many aneurysms—the collected figures from various sources make this clear. The possible methods of treatment are briefly described and illustrated by several case reports. The authors also describe and evaluate the various methods of storing vascular grafts.

Bronchogenic Carcinoma: Cell Type and Other Factors Relating to Prognosis. J. W. Kirklin, J. R. McDonald, O. T. Clagett and others. Surg., Gynec. & Obst. **100:**429-438 (April) 1955 [Chicago].

The records of patients in whom a diagnosis of lung cancer was made at the Mayo Clinic during the years 1943 to 1949 were reviewed. All patients in whom it appeared that the lung cancer was metastatic were omitted, leaving 1,577 cases presumed to be cases of primary cancer of the lung. The authors review 844 cases in which they were able to reexamine the tissue histologically. Of these patients 64 or 7.6% had adenoma of the bronchus, 10 had alveolar cell tumor, and 3 could not be classified. The authors are concerned chiefly with the 767 patients (90.9%) who had bronchogenic carcinoma. They classify primary bronchogenic carcinoma into four groups on the basis of the cell type. Operability rates, resectability, and survival rates are presented for each of the four cell types of bronchogenic carcinoma: squamous cell carcinoma, adenocarcinoma, large cell carcinoma, and small cell carcinoma. The authors regard as a squamous cell carcinoma only those neoplasms in which the carcinoma cells show evidence of epidermization, namely, the production of keratin, cornified epithelium, or prickle cells. The adenocarcinomas produce glands or secrete mucus. They should be differentiated from metastatic carcinoma and from alveolar cell carcinoma. A small cell bronchogenic carcinoma is a tumor in which the cells are small (about one and a half times the size of a lymphocyte) with a deeply staining nucleus and little cytoplasm. Sometimes the cells with their nuclei are spindle shaped; this characteristic has given rise to the name "oat cell" carcinoma. The large cell bronchogenic carcinoma is a tumor in which the cells are undifferentiated. Some pathologists classify some of these carcinomas with the squamous cell carcinomas and classify others with the small cell carcinoma and term them "undifferentiated carcinomas." The authors believe that this group should be segregated. In 369 of the 767 cases of primary bronchogenic carcinoma reviewed, thoracotomy was performed, giving an exploration rate of 48%. Resection was effected in 184 cases (49.8% of the cases in which exploration was carried out), or in 24% of the 767 cases. The five year survival rate in those undergoing curative resection was 37%. The survival rate following resection for adenoma of the bronchus is excellent. The inclusion of such cases in a series of bronchogenic carcinoma would result in a survival rate higher than would be obtained for pure primary bronchogenic carcinomas. The authors found that the cell type is an important factor in prognosis in cases of primary bronchogenic carcinoma. Patients with adenocarcinoma and squamous cell carcinoma have a relatively good prognosis provided resection is possible. Resection is possible in a higher percentage of cases than it is in cases of the large cell and small cell carcinoma. The prognosis from surgical treatment of small cell carcinoma is poor, since resection is possible in only about 1 case in 10 and the survival rate following resection is exceedingly low. Since there is at present no other useful form of treatment for small cell carcinoma, resection must be attempted whenever feasible. The small chance for cure makes heroic procedures of doubtful advisability in this group of cancers. However, the survival following resection for adenocarcinoma and squamous cell carcinoma encourages extensive operations for these lesions when necessary, if by them all the gross tumor can be removed. Similar procedures seem justified in cases of large cell carcinoma, although the rewards will not be as great.

Late Results Following Pneumonectomy and Lobectomy for Bronchogenic Carcinoma. H. R. Sørensen and F. Therkelsen. Acta chir. scandinav. **108:**375-392 (No. 5) 1955 (In English) [Stockholm, Sweden].

Factors to be considered in evaluating the results of surgical therapy in lung cancer are the operability rate, the operative mortality, the survival time, and the amount of postoperative disability. An increase in the operability rate from 26.7% for the 1942-1949 period to 38.9% for the period from 1950 to September, 1953, is shown in the authors' series, and similar increases have been reported by other workers. Earlier diagnosis and advances in surgical treatment, such as extrapleural dissection; resection of the diaphragm, pericardium, and atrium; and a wider use of thoracotomy, are among the principal causes of the increase, but in spite of the progress that has been made, the present operability rate is not high enough; there must still be many patients in whom the diagnosis could be made at an earlier stage. The operative mortality in the authors' series dropped from about 30% in the early years to 11.3% in 1953, when only 5 of the 44 patients operated on died. The causes of this decline, apart from increasing experience, are undoubtedly improvements in anesthetic technique, the prophylactic use of antibiotics, and the institution of breathing exercises. The decline in the number of deaths due to bronchial fistulas, infections, and cardiac complications was considerably more than the over-all figures for the series suggest, because pulmonary embolism was a more common cause of death in the later years. Analysis of the results in relation to the type of operation performed shows that the mortality rate will be lower when the operation can be restricted to lobectomy. The indications for lobectomy in most cases were a lesion so localized that lobectomy could be considered a radical procedure; occasionally, however, the patient's advanced age and poor general condition were the deciding factors. The mortality rate for patients over 60 (21%), though twice as high as that for those under 60, is not high enough to contraindicate surgical treatment. The unusually high five year survival rate of 40% in this series may be explained by the fact that it contained a relatively large number of cases of squamous-cell carcinoma and comparatively few cases of lymph-node metastases. The best results were obtained in the patients who were under 60 and had squamous-cell carcinomas without lymph-node metastases; in this group the five year survival rate was 73%. Some prognostic factors cannot be influenced by early diagnosis or improved therapeutic methods. One such factor is the histological type of the tumor; thus the prognosis for anaplastic carcinoma is extremely poor. Follow-up of 22 patients, with an observation period of from four to nine years, showed that the 5 who had had lobectomies were performing their usual work without difficulty and that 12 of those in whom pneumonectomy was performed had resumed their previous jobs, although 2 were doing less work than before. One of the remaining five had a lighter occupation, and four, whose employment had required heavy physical work, were unemployed.

Sensitivities of Ten Species of Clostridia to Penicillin, Aureomycin, Terramycin, and Chloramphenicol: A Study of Battle Wounds in Korea. A. Newton, J. G. Strawitz, R. B. Lindberg and others. Surgery **37:**392-399 (March) 1955 [St. Louis].

Throughout the latter part of the Korean conflict, penicillin (300,000 to 600,000 units) was administered intramuscularly as the soldier reached the battalion aid station. Following operation, casualties routinely received penicillin (300,000 units) every 12 hours. In addition, casualties with intraperitoneal injuries, arterial injuries, or intrathoracic injuries received 0.5 gm. of streptomycin every 12 hours. Chlortetracycline (Aureomycin) was available but was used infrequently. In a previous study, 11 wounds inflicted during the Korean conflict were examined bacteriologically throughout the first week of healing. This was done by culture of tissue excised from the open wound at the time of primary débridement and every two days thereafter during the ensuing week. Fifty-six clostridial isolates and numerous aerobic organisms were obtained. In this study the sensitivities of the clostridial isolates to penicillin, chlortetracycline (Aureomycin), oxytetracycline (Terramycin), and chloramphenicol are presented and correlated with human serum levels of these antibiotics. Within the limitations of the in vitro sensitivity method, chlortetracycline and oxytetracycline would appear to be the drugs of choice in preventing or treating clostridial wound infections. As an adjunct to débridement, however, all four of the antibiotics included in this study appear to be beneficial in preventing or minimizing clostridial infections. Experimental studies have shown that the concentrations of most antibiotics in the muscle are less than concentrations found in the serum. If the time should ever come again when, as a compromise, antibiotic therapy must be used as a bulwark to support delayed surgery of mass casualties, increased dosages of these drugs might be in order.

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Determining the Site of Brain Tumors: Use of Radioactive Iodine and Phosphorus. E. W. Amyes, P. H. Deeb, P. J. Vogel and R. M. Adams. California Med. **82**:167-170 (March) 1955 [San Francisco].

Certain pathological disturbances in the brain, e. g., tumors, inflammations, and vascular diseases, tend to increase the rate of passage of some ions across the so-called blood-brain barrier. If these ions are made radioactive their presence can be detected by sensitive instruments. In tumors, there may be additional factors at work; increased metabolic activity, for example, might cause the phosphorus ion to concentrate. With the use of radioactive iodine combined with diiodofluorescein, the site of tumors was correctly determined in 61% of 39 cases of tumors of the cerebral hemispheres. In 19 cases in which the focal radioactivity was increased 24% or more over that of the surrounding area, there were no errors in localization. Fifteen patients with expanding intracranial lesions were tested at operation with radioactive phosphorus and 14 lesions were correctly localized. The one failure was in a case of abscess. This test uses a needle Geiger tube. It seems probable that only in those cases in which the tumor is in the lateral portion of the cerebral hemispheres and is of sufficient size will the radioisotope test be of value in localizing the lesion. It is usually possible by other means, e. g., ventriculography or angiography, to determine whether or not the tumor is in the cerebral hemispheres. The radioisotope test has not proved valuable in localizing posterior fossa or midline neoplasms. The test appears to be of help in screening groups of persons who are suspected of having organic intracerebral disease; a focus of increased radioactivity should arouse a strong suspicion that a neurological lesion is present. The authors believe the use of radioactive phosphorus to be a useful adjunct to the other means of locating a tumor at the time of operation. The tumor can often be found more rapidly and with less trauma to the brain. In certain cases it is possible to find the lesion and obtain a specimen for biopsy through a solitary burr hole. If the lesion is highly malignant and deep, major craniotomy can thus be avoided. The technique in which radioactive phosphorus is used to localize tumors during operation has been found to be very accurate. However, the authors believe this latter procedure deserves a place in the study of intracerebral tumors as well as other types of brain disease. At present the accuracy of the results achieved preoperatively is not great enough to allow its use alone in determining the site of the pathological process. However, the presence of a focus of increased activity above 20% in the series of patients studied at the White Memorial Hospital, Los Angeles, always indicated the correct location of the lesion in cases of tumor.

Chronic Spinal Epidural and Subdural Hematoma: Report of Three Cases and Review of Literature. Medicina **14**:379-398 (Dec.) 1954 (In Spanish) [Buenos Aires, Argentina].

Three cases of chronic intraspinal hematoma are reported. The first patient, a child 4 years old, had a minor spinal trauma on the dorsal region, followed in 10 days by appearance of symptoms of medullary compression with early occurrence of spastic paresis. Myelography and an operation were made on the ninth day after appearance of the neurological symptoms. There was myelographic partial blockage from the 5th to the 10th dorsal vertebrae. The operation consisted of laminectomy and removal of a well-organized hematoma 6 mm. thick that occupied the epidural space in an extension of four vertebrae, at the seat of the blockage. The dura mater began to pulsate as soon as the hematoma was resected. Its inner surface was normal. Neurological recuperation followed, and it was complete at the end of six months. The second patient was an infant 4 months old. He was born in breech presentation with traumatizing maneuvers. Congenital paraplegia showed immediately after birth. Myelography and an operation were done when the patient was 4 months old. There was almost complete myelographic blockage between the ninth dorsal and first lumbar vertebrae. The operation consisted of laminectomy and removal of two well-organized hematomas, one extradural and one subdural, that occupied the spinal canal from the ninth dorsal to the first lumbar vertebrae. Recuperation was minimal two months after the operation. The third patient was a man 51 years old who had two operations under spinal anesthesia. A syndrome of medullary compression of all the dorsal column appeared one year after the last operation. It followed a rapid course, with paralysis of the legs, incontinence of urine, and disorders of sensation and sensibility of the lower half of the body. The operation consisted of laminectomy, longitudinal opening of the dura mater, and partial removal of a large hematoma 3 mm. thick. Its upper limit was on the third dorsal vertebra. The distal limit was not determined. The macroscopic aspect and histological structure of the hematoma were those of hemorrhagic internal pachymeningitis. No improvement followed the operation. The patient refused to have another operation. The authors conclude that chronic spinal extradural hematoma produces a syndrome of dorsal medullary compression with early paresis. It shows by myelographic blockage of an extradural type. It is promptly organized with a capsule and occupies a segment of four or six vertebrae. Operation is indicated. It consists of removal of the hematoma and its capsule. Neurological recuperation is in direct relation to time of the operation and in inverse relation to the acuteness of the medullary lesion caused by compression. Chronic spinal subdural hematoma is extremely rare. Its macroscopic aspect and histological structure are those of hemorrhagic internal pachymeningitis. Its final stage of sclerosis elicits a dural reaction, with consequent development of hypertrophic pachymeningitis. Congenital paraplegia is due to obstetric trauma. It may result either from elongation of the spinal cord during traction of the fetus in prolonged labor, especially if the fetus is in breech presentation, or from medullary compression by an epidural and/or subdural hematoma. When the disease is due to medullary compression, as shown by myelographic blockage, early surgical evacuation of the hematoma results in recovery. In all cases of congenital paraplegia, myelography should be made a few hours or a few days after birth, immediately followed by an operation, if indicated.

Prostigmine-Induced Muscle Weakness in Myasthenia Gravis Patients. L. P. Rowland, M. C. Korengold, I. A. Jaffe and others. Neurology **5**:89-99 (Feb.) 1955 [Minneapolis].

According to Rowland and associates muscular weakness has been reported in patients with myasthenia gravis that is attributed to overtreatment with anticholinesterase rather than to the disease itself. The authors decided to investigate whether neostigmine (Prostigmine) can cause weakness in myasthenia gravis patients. There are many patients who are neither completely nor continuously free of symptoms; there are also some who improve initially but whose symptoms later seem to become refractory to the beneficial effects of the drug; and there are even some who seem to have myasthenia gravis but never respond to the drug. For any of these patients whose symptoms are incompletely controlled, the question arises whether increased amounts of neostigmine (Prostigmine) would be beneficial or dangerous. Four patients with myasthenia gravis were studied. Each of them had a characteristic history and responded to prostigmine to some degree. Intravenous infusions of prostigmine methylsulfate were administered in gradually increasing amounts, starting with 1 mg. per hour. The concentration of the drug in isotonic sodium chloride solution was such that 100 cc. of fluid was usually given each hour. No patient received more than 500 cc. in the course of an infusion lasting less than five hours. Except where otherwise indicated, 0.1 mg. of atropine sulfate was added to the solution for each 1 mg. of prostigmine. This amount was usually sufficient to prevent the appearance of muscarinic symptoms, but supplemental doses of atropine were sometimes necessary. No patient received more than 2 mg. of atropine during a single infusion of prostigmine. The intravenous administration of large amounts of neostigmine produced weakness in patients with myasthenia gravis. Prostigmine-induced weakness was usually preceded by improvement in clinically weak muscles, but the improvement was usually incomplete. There was no consistent pattern of weakness, but muscles that had not been clinically weak previously were usually affected simultaneously with "myasthenic" muscles. Muscarinic

symptoms were not present at the time of weakness when atropine was administered with the prostigmine; fasciculation was present in some patients but not in others. Recovery after prostigmine-induced weakness was rapid.

PEDIATRICS

Congenital Pyloric Stenosis in Older Babies. J. Rendle-Short and R. B. Zachary. Arch. Dis. Childhood **30:**70-71 (Feb.) 1955 [London, England].

Rendle-Short and Zachary present the histories of two infants in whom the symptoms of congenital pyloric stenosis did not appear until they were 5½ months and 3 months old, respectively, whereas the symptoms of this congenital defect usually become evident between the second and sixth week of life. These two cases and one reported in 1935 by French investigators show that congenital pyloric stenosis may occur in babies over the normally accepted age, and therefore the diagnosis should not be discounted solely on this score. It is not clear why children predisposed to pyloric stenosis should begin to vomit at any particular time, but there are probably two factors involved: hypertrophy of the pyloric muscle decreases the lumen of the canal, and at the same time, the caliber of the gut, including the pylorus, increases as the child grows. The critical phase comes when the muscle of the pylorus has hypertrophied but its lumen is still quite small. Obstruction can then readily take place, especially if edema of the gastric mucosa develops either as the result of infection or from mechanical irritation. In older babies, in whom the lumen of the pyloric canal is larger, as is indicated by the flabbiness of the tumor palpated at operation, perhaps greater mucosal swelling is required before symptoms develop. This may account for the rareness of the condition in older infants. It is of interest that one of the two infants reported had otitis media on admission, and an upper respiratory infection may have precipitated the onset of vomiting.

UROLOGY

Effect of Testosterone Propionate on the Prostate Gland of Patients Over 45. M. A. Lesser, S. N. Vose and G. M. Dixey. J. Clin. Endocrinol. **15:**297-300 (March) 1955 [Springfield, Ill.].

One hundred men over 45 years of age, previously treated for angina pectoris or the male climacteric with amounts of testosterone propionate not exceeding 5,200 mg., were examined. The incidence of prostatic abnormalities among them was compared to that in another 100 men over 45 who had never received testosterone propionate. Prostatic abnormalities had developed in 32 patients of the treated group, but similar abnormalities had developed in 39 of the controls. Prostatic hypertrophy was present in 27 of the treated patients, but 34 control subjects also had enlarged prostate glands. Palpable prostatic irregularities occurred in 11 treated patients and in 13 controls. Carcinoma of the prostate was found in one man, an 80-year-old patient of the treated group, seven years after the end of treatment. Thus in this study there was no evidence that testosterone propionate in the dosage used had initiated carcinoma or had activated latent carcinoma of the prostate gland.

Some Uses of an Isolated Loop of Ileum in Genito-Urinary Surgery. L. N. Pyrah and F. P. Raper. Brit. J. Surg. **42:**337-357 (Jan.) 1955 [Bristol, England].

Pyrah and Raper present 13 cases in which an isolated loop of lower ileum was used to enlarge a contracted bladder, to relieve at the same time a contracted bladder and a hydronephrosis of a solitary kidney, to reanastomose ureters previously transplanted into the colon to the bladder, to replace part of a ureter excised for neoplasm, or to act as an artificial bladder. They show that the lower ileum is singularly convenient for incorporation into the urinary tract. It has an excellent blood supply arranged in arcades, the transverse part of which can be divided without impairing the vitality of the intestine; the ileal mesentery is in effect a long pedicle that allows the ileum to lie without tension in any part of the pelvis. Its peristaltic contractions are vigorous and continue to act even when a segment of the ileum is isolated. Its secretive and absorptive properties must be carefully considered if it is to be used to transport urine. Although experiments have indicated that an ileal loop may absorb an excess of potassium from urine, there have been few clinical reports of such chemical imbalance occurring in patients who have had an ileal loop incorporated in some part of the urinary tract. The method of isolation of the ileal loop is common to all of these operations. Prior to operation the patient receives a low-residue diet, together with either 5 mg. of streptomycin in 100 ml. of water daily by mouth or 250 mg. of chlortetracycline (Aureomycin) every four hours on the four days before operation. The colon is washed out on the two mornings before operation and an enema given on the evening before operation. When the abdomen has been opened, a suitable coil of intestine in the lowest 3 ft. of the ileum is selected. The intestine must be healthy and must have a mesentery sufficiently long to reach the bladder without tension. The rest of the small intestine is then pushed into the upper abdomen and retained there by moist packs; this procedure is aided by putting the patient in a moderate Trendelenburg position. If the ureters are to be anastomosed to the ileal loop, these are now isolated and prepared. Once this has been done, a more accurate estimation can be made of the length of ileal loop required. At the lower point selected for division of the ileum, which should be about 10 cm. above the ileocecal valve, the vascular arcade close to the intestine is divided between ligatures and the cut is prolonged into the mesentery at right angles to the intestine. The mesentery rarely needs to be cut for a distance exceeding 5 cm. The base of the mesentery to the isolated loop should be as wide as possible in order to minimize the chance of rotation of the vascular pedicle. The intestine is divided between clamps at the two selected places and continuity of the intestine restored by lateral or end-to-side anastomosis. Pyrah irrigates the isolated loop with sterile isotonic sodium chloride solution, thereby evacuating bile-stained fluid and debris. The further preparation of the loop depends upon the use to which it is to be put. For one type of ileocystoplasty the two ends are closed and the anastomosis to the bladder is made at the center of the loop. For another method of ileocystoplasty, the loop is completely opened. Ileoplasty using a closed loop is an easier operation to perform than the attachment of an opened loop of ileum to the partially resected bladder. The operations on the ureters and the use of the ileum as an artificial bladder are also described and the histories of the patients in whom they were used are presented.

A True Hermaphrodite. G. W. Schwiebinger and C. V. Hodges. J. Urol. **73:**424-429 (Feb.) 1955 [Baltimore].

The patient described was first seen by Schwiebinger and Hodges because of penoscrotal hypospadias and right cryptorchidism. He was then a normal-appearing 5-year-old boy. A moderate amount of chordee and a penoscrotal hypospadias were present. The left testis was in the scrotum and appeared normal to palpation. The right testis could not be palpated in the scrotum or in the inguinal canal. It was elected to correct the hypospadias first. At the age of 7½, a Denis Browne type of hypospadiac repair was performed. At the age of 9 the patient was readmitted for right orchiopexy. His urethroplasty had healed and was functioning well. A right indirect inguinal hernia was present, but no gonad was palpable. The right inguinal canal was exposed, and an indirect hernial sac was identified. When traction was applied, a normal, cystic-appearing ovary and fallopian tube with fimbriate end presented. Incision into the scrotum was then performed. A normal appearing testis with a fibrotic epididymis and vas deferens was found along with another fallopian tube with a fimbriate end. Laparotomy revealed only a pseudopouch of Douglas; no other female structures were found. Frozen section confirmed the gross impressions about each gonad. A right salpingo-oophorectomy and herniorrhaphy were performed, as well as a left salpingectomy. Paraffin sections of the surgical specimens revealed an immature testis, normal fallopian tubes, and a well-differentiated ovary. Cystoscopy performed during the patient's convalescence revealed the absence of the verumontanum and prostate, but a

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vaginal orifice opened into the area where the utricle would normally be found. Three months later, colpectomy was performed. The authors stress that the clinical diagnosis of hermaphroditism may be made definitely only by histological evidence of the coexistence of ovarian and testicular tissue. A hypospadiac phallus is a common finding, although normal external genitals do occur. As one or more of the gonads are usually found intra-abdominally, the external genitals may resemble either the female labia or the male scrotum with cryptorchidism. Inguinal hernias are frequently found. As the pragmatic sex is somewhat difficult to determine, especially in the youth, treatment is directed toward development of the genetic sex. This necessitates exact diagnosis by examination of both gonads microscopically, laparotomy to determine presence or absence of accessory reproductive organs, and cystoscopy to evaluate that portion of the genital tract. Ideally these procedures should all be carried out prior to extirpation of either gonad and the situation discussed with the parents. The case described induced the authors to study previously reported cases, and they were impressed with the frequency of hypospadias and cryptorchidism. They recommend urethrocystoscopy in all cases where this unusual combination exists and feel that this problem should be thought of when cryptorchid repair is done. If the parents are told in advance that abnormalities of this type do occur in the cryptorchid gonad, laparotomy may then be performed if indicated, the entire story unfolded, and appropriate surgical therapy instituted at a single session.

Problem of Injury to Lower Vena Cava During Nephrectomy. O. Hennig. Ztschr. Urol. **48:**1-16 (No. 1) 1955 (In German) [Leipzig, Germany].

Hennig emphasizes that if in the course of a difficult nephrectomy the vena cava is injured, the surgeon must give his complete attention to this injury. The more rapidly the surgeon effects provisional arrest of hemorrhage by manual compression of the vena cava, the less is the danger of fatal hemorrhage. Immediate definitive repair of the injured vena cava by suturing the vessel is the method of choice. Provisional hemostasis with gauze roll compresses is unreliable, and the transverse ligation of the vena cava is dangerous; if a rent is at the level of the left renal vein, such ligation is incompatible with survival. Hennig feels that prolonged tamponade by packing with a gauze roll is a mistake. In this connection he evaluates critically a case reported in 1953 by other surgeons, in which repair of a rent in the vena cava was carried out belatedly, that is, 18 days after the nephrectomy. He believes that the patient was lucky to survive the heroic operation and that late repair should not become the rule, since the operation is too trying for the weakened patient. The urologic surgeon should completely master the technique of vascular suture, particularly that of the vena cava.

THERAPEUTICS

Bioassay of the Diuretic Potency of Xanthines and the Organic Mercurials in Patients with Congestive Failure. T. Greiner, H. Gold, F. Palumbo and others. J. Pharmacol. & Exper. Therap. **113:**140-147 (Feb.) 1955 [Baltimore].

Surveys suggest that xanthine materials are more often included in prescriptions written by physicians than any other diuretic agent, but their place in diuretic therapy in relation to other agents used for this purpose is still unsettled. Satisfactory methods for quantitative comparisons have not been available. A method for the bioassay of diuretic agents in ambulant patients with congestive failure has been developed by Greiner and co-workers. It yields comparisons that can be verified by statistical techniques. In the present study this method has been applied for the purpose of comparing the potency of aminophylline with meralluride (Mercuhydrin), to determine the degree to which the diuretic action of Mercuhydrin may be augmented by aminophylline, to compare the diuretic action of aminophylline by intramuscular and oral administration, and to compare the therapeutic value of orally given theophylline in the form of the ethylenediamine with that of the calcium salt. It was established that a large intramuscular dose, 0.5 gm. of aminophylline, causes a diuretic effect equal to that of 0.6 ml. of Mercuhydrin by intramuscular injection. Aminophylline is somewhat less effective by the oral route. In terms of molecular weight, aminophylline and calcium theophyllinate have equal diuretic potency. This raises a question concerning the difference in absorption of the two materials, since one contains twice as much theophylline as the other. Aminophylline may enhance the diuretic activity of the organic mercurials by approximately 50%. In contrast to the case of ammonium chloride, the result does not represent potentiation but simple summation or less than summation. While there is ample evidence that aminophylline can boost the diuretic response with suboptimal dosage plans of the mercurials, the proof is not sufficient for the assumption that the xanthines will restore diuretic response in patients with conditions refractory to the organic mercurials.

Successful Calcium Disodium Ethylene Diamine Tetra-Acetate Treatment of Lead Poisoning in an Infant. L. A. Kneller, H. S. M. Uhl and J. Brem. New England J. Med. **252:**338-340 (March 3) 1955 [Boston].

A 20-month-old boy was treated for plumbism with encephalopathy with a solution consisting of 0.5 gm. of calcium disodium ethylenediaminetetraacetate (CaEDTA) in 100 cc. of isotonic sodium chloride solution given by subcutaneous clysis. Both thighs and the subscapular areas of the back were chosen as the sites of injection. At first hyaluronidase was used, but rotation of the sites of injection obviated the necessity for the enzyme. The clyses, administered three times daily for five days, were given over a one-hour period, and the absorption occurred between one and a half and two hours. There was neither local tissue damage nor reaction, and the patient tolerated the procedure well. This method is considered the best for the administration of CaEDTA, which is the drug of choice in lead intoxication. The clinical response to this therapy was dramatic and correlated well with the marked increase in the urinary excretion and the fall in the blood level of lead observed in the patient at this time. An unusual feature of the case was the occurrence of hypercalcemia at the time of CaEDTA therapy, in association with signs and symptoms of central nervous system dysfunction. The clinical findings were not characteristic of either hypocalcemia or hypercalcemia. It is possible that the high serum calcium level was due in part to a rapid exchange for readily available lead cations, thus freeing calcium ions into the plasma. It seems that the event was of no serious pathological significance. When seen one year after the episode, the patient's general health was excellent, but there was some retardation of speech.

Bacteriology and Pharmacology of Benzoyl-Para-Aminosalicylic Acid. G. Schönholzer, H. Lauener and H. Hurni. Schweiz. med. Wchnschr. **85:**222-228 (March 5) 1955 (In German) [Basel, Switzerland].

The calcium salt of N-benzoyl-*p*-aminosalicylic acid (Benzacyl), a new *p*-aminosalicylic acid (PAS) derivative, was tested bacteriologically and pharmacologically with regard to its suitability as a tuberculostatic agent. Despite the relationship of Benzacyl with *p*-aminosalicylic acid, several of its properties differ from those of the latter drug. 1. The tuberculostatic effect in vitro of Benzacyl is on the average 75 times weaker than that of *p*-aminosalicylic acid. Results of experiments in mice and guinea pigs that were infected intravenously with 0.25 cc. of a suspension of Mycobacterium tuberculosis showed that a dose of Benzacyl, the total weight of which equaled that of a dose of *p*-aminosalicylic acid, was equally effective. 2. In vitro, Benzacyl exerts almost the same effect against *p*-aminosalicylic acid-resistant strains of Myco. tuberculosis as against strains of this pathological agent that are normally sensitive to *p*-aminosalicylic acid. Para-aminobenzoic acid does not abolish the tuberculostatic effect of Benzacyl. Concentration of free *p*-aminosalicylic acid in the blood proved to be low after the oral administration of Benzacyl. These three facts suggest that the effect of Benzacyl depends primarily on the compound as such and not on the splitting up of *p*-aminosalicylic acid. 3. Benzacyl

when given parenterally is somewhat more toxic than *p*-aminosalicylic acid. Tolerance of animals to orally given Benzacyl is about the same as that to orally given *p*-aminosalicylic acid, while tolerance of man to orally given Benzacyl is definitely better than that to orally given *p*-aminosalicylic acid. 4. Benzacyl is absorbed and excreted relatively slowly, with the result of a balanced concentration of the drug in the blood. There is no risk of a cumulative effect. 5. According to clinical reports, Benzacyl in doses of from 4 gm. given three times daily to 6 gm. given three times daily delays or prevents resistance to isoniazid and streptomycin in the same way that *p*-aminosalicylic acid does.

Penicillin Anaphylaxis: Case Report. L. M. Morrisset. Texas J. Med. **51:**77-78 (Feb.) 1955 [Austin, Texas].

The patient whose case is reported, a man aged 39, was given an injection of 400,000 units of procaine penicillin into the deltoid muscle when he complained of a sore throat and running nose. There was no history of allergy, but he had received about 12 injections of procaine penicillin, the last about 30 days previously. Approximately one minute after the penicillin had been injected the patient complained of tingling all over, vomited twice, stated he "couldn't breathe," and collapsed. The blood pressure and pulse were unobtainable. Respiration was gasping, and a few high pitched rales could be heard, but there was no normal breath sounds. The patient became incontinent. One cubic centimeter of epinephrine in 1:1,000 solution was given intramuscularly. One hundred milligrams of cortisone in 300 cc. of isotonic sodium chloride solution was given intravenously. Oxygen administration was started. Intermittent injections of epinephrine were given in doses of 0.5 to 1.5 cc. intravenously at periods of three to five minutes. One hour later the patient was still cyanotic, with blood pressure of 60/30 mm. Hg, but he had regained consciousness enough to state that he felt better. After the cyanosis had subsided, he felt much better but was very weak and his joints were sore. His tongue and upper lip were swollen. Oxygen administration was discontinued, and the patient did not require further treatment. Physicians should anticipate, recognize, and immediately treat these potentially fatal reactions. In some of the cases reported in the literature epinephrine has played a dominant role in the recovery. It has also been recommended that this drug be given intravenously because of the profound circulatory collapse. Intravenously given cortisone seemed to be of definite benefit in this case. The oxygen was of no use until the obstruction was relieved at the level of the bronchioles. Adherence to the following recommendations may prevent reactions to penicillin: (1) stopping the indiscriminate use of penicillin preparations, especially lozenges, ointments, gargles, tooth pastes, and gums; (2) protecting patients who are sensitive by giving them cards stating they are sensitive; (3) interrogating patients concerning penicillin sensitivity before using penicillin therapy; and (4) using a skin test in persons suspected of being sensitive to penicillin.

Ambulatory Continuous Drip Method in the Treatment of Peptic Ulcer. F. Steigmann and E. Goldberg. Am. J. Digest Dis. **22:**67-71 (March) 1955 [Fort Wayne, Ind.].

Nulacin, a new proprietary antacid tablet for oral administration that dissolves slowly and that contains solids from whole milk, combined with dextran and maltose, magnesium trisilicate, magnesium oxide, calcium carbonate, magnesium carbonate, and peppermint oil was given to 46 patients between the ages of 17 and 70 years with gastroduodenal ulcer or hypertrophic gastritis. Twenty-seven of the 46 patients had been previously treated and were started on the new therapy because of an exacerbation or recurrence of symptoms; the remaining 19 patients had been designated intractable because they did not respond to a previously instituted medical regimen. All patients were put on a regimen of ambulatory medical management with the exception of four who were in the hospital when the treatment was started. The patients were advised to keep a tablet in their mouth at all times during their waking hours, except while eating. They also were advised not to chew or swallow the tablet and not to move it from side to side. Antispasmodics and sedatives were ordered three times daily and at bedtime. The patients were advised against alcoholic beverages, coffee, and smoking. Whenever indicated, psychiatric consultation was utilized. Most patients took 12 to 14 tablets daily; the tablets are so prepared that they dissolve slowly over a period of 25 to 60 minutes. In almost all patients who were started on this regimen of continuous antacid therapy gastric symptoms improved. In some the pain was relieved promptly, while others had some pain intermittently at first. The taking of a tablet at bedtime prevented previously occurring night pain in some patients. As their symptoms improved, patients began to cut down on the number of tablets taken per 24 hours. Of the 46 patients 10 were followed up for less than three months, while 36 were followed up for from 5 to 15 months. Some of the patients took only up to 6 tablets daily in the latter part of the observation period, and, at times, they did not take any tablets for days. Only 10 patients continued to take 10 to 12 tablets daily for up to eight months. There seemed to be little objection to the keeping of these antacid tablets in the mouth, or to the frequency with which they had to be taken. Only minor side-effects, such as nausea because of the sweetish taste of the tablets, a burning sensation in the throat, and a bad taste in the mouth, were noted. This mode of administering antacid "ambulatory drip therapy" seems to offer a new, highly effective approach in the treatment of patients with peptic ulcer. The main indication for this new antacid therapy is in patients with acute ulcer exacerbation and its associated severe pain. In these latter patients, the constant swallowing of a saliva mixed with alkali seems to greatly alleviate the upper abdominal distress. The lack of any intestinal disturbance—constipation or diarrhea—in these patients is another factor in favor of ulcer therapy with this new antacid tablet.

Therapeutic Value of Tetracycline. A. Ravina, M. Pestel, Y. Trocmé and R. Albouy. Presse méd. **63:**263-264 (Feb. 23) 1955 (In French) [Paris, France].

The results obtained with tetracycline in a wide variety of infectious conditions seem to show that it is the most effective of the recently developed antibiotics. It is easy to administer; its action is rapid; and it is effective against most strains of staphylococci. It was used successfully by the authors in patients with acute and chronic pulmonary disease, urinary infections, typhoid fever, and staphylococcic infections of various kinds. Most of the patients were given 500 mg. of the drug orally in the morning and again 12 hours later in the evening, and this dosage, which was always sufficient, was never exceeded. A few patients with especially severe infections were given intramuscular injections of 100 mg. morning and evening, with results that were exactly the same as those produced by the oral administration of 1 gm. daily. These doses could apparently be largely exceeded, if necessary, because of the low toxicity of tetracycline. Side-effects are seldom seen, and those that do appear are usually benign. Some patients complain of nausea, and diarrhea may be profuse, but on the whole gastrointestinal tolerance seems to be better for tetracycline than for aureomycin and terramycin. Tolerance for antibiotics is often poor in elderly patients, especially when their use has to be continued for any length of time. Intramuscular injections soon become painful in such cases, and they may even serve as starting points for acute or subacute infections. The fact that tetracycline can be administered orally and that it acts rapidly therefore makes it particularly valuable in the treatment of aged and infirm patients.

Anticoagulant Therapy of Cardiac Infarct. W. Löffler and M. Schnebli. Deutsche med. Wchnschr. **80:**305-308 (March 4) 1955 (In German) [Stuttgart, Germany].

Of 300 patients with acute myocardial infarction who were admitted to the medical clinic of the University in Zürich, Switzerland, 200 were treated with anticoagulants and 100 did not receive such treatment. Since thromboembolic complications usually occur only toward the end of the first week after the infarction, anticoagulant therapy of patients with definitely recent infarcts was instituted with 6 tablets (18 mg.) of 3-(1-phenylpropyl)-4-hydroxycoumarin (Marcoumar) on the first day, and 2 to 3 tablets (6 to 9 mg.) were given on the second day to

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reduce Quick's prothrombin time from 100% to about 20%. The prothrombin time may then be maintained at this level with 1.5 to 4.5 mg. of Marcoumar daily. It is indispensable to perform Quick's prothrombin time test daily since the sensitivity of the individual patient to Marcoumar varies considerably. Patients with not definitely recent infarction were given combined treatment with Marcoumar and a proprietary preparation of pure heparin (Liquemin); the latter drug was administered in doses of 150 mg. three to four times daily, i. e., 15,000 units per day. Liquemin was discontinued when the optimal prothrombin time was obtained with Marcoumar. Forty-eight (24%) of the 200 treated patients died, as compared to 73 (73%) of the 100 untreated patients. Not one of the 48 treated patients died of pulmonary, cerebral, or renal embolism, while 13 of the 73 patients died of pulmonary embolism and 11 of cerebral or renal embolism, i. e., one-third of the untreated fatal cases. Venous complications, as well as arterial embolism originating from the heart, did not occur in patients who received optimum anticoagulant therapy, while 41 such incidents occurred among the patients who did not receive anticoagulant treatment. Of a group of 34 patients between the ages of 60 and 70 years, i. e., in the age groups in which the incidence of myocardial infarction is highest, 17 were treated with anticoagulants and the other 17 were not. Of the 17 treated, 14 were improved and 3 died, while of the 17 untreated patients 4 were improved and 13 died. These results clearly show the favorable effect of the anticoagulant treatment in a group of patients whose clinical condition was to a large extent the same. Contraindications to anticoagulant therapy consist of hemorrhages and of tendency to bleeding, as in patients with gastric ulcer. Except for these contraindications, coagulation therapy should no longer be withheld from patients with myocardial infarction. A definitely favorable effect of anticoagulant therapy on the local phenomena of infarction or a lower incidence of secondary infarction, however, could not be demonstrated, but only four patients (2%) died from secondary infarction in the treated groups, as compared to five (5%) in the untreated group. Because of the great latitude of variations in the disease process of myocardial infarction, the authors consider their data more convincing than those obtained from questionnaires. In contrast to American workers, the authors do not believe that only "poor risk" patients should be treated with anticoagulants. "Good risk" patients may become "poor risk" patients in the course of a few days. The authors never used "armchair" treatment but always strict bed rest, and for that reason they consider anticoagulant therapy indicated in "good risk" patients as well as in the others.

Fluorohydrocortisone and Chlorohydrocortisone, Highly Potent Derivatives of Compound F. A. Goldfien, J. C. Laidlaw, N. Abu Haydar and others. New England J. Med. **252:**415-421 (March 17) 1955 [Boston].

Metabolic and therapeutic studies with chlorohydrocortisone and fluorohydrocortisone indicate that the insertion of a chlorine or fluorine atom at the 9-alpha position of hydrocortisone greatly potentiates both the metabolic activity and the duration of action of the parent compound. Of the two derivatives, fluorohydrocortisone is the more potent. Preliminary studies indicate that the ratio of mineralocorticoid to glucocorticoid activity is somewhat greater for fluorohydrocortisone than for hydrocortisone. Both chlorohydrocortisone and fluorohydrocortisone have been successfully used as the sole maintenance therapy in patients with adrenal cortical hypofunction (Addison's disease). Satisfactory inhibition of the adrenal cortex has been achieved with doses of 1 or 2 mg. of fluorohydrocortisone by mouth a day in normal subjects and in women with the adrenogenital syndrome. In a patient with a mixed clinical picture due to bilateral adrenal hyperplasia, adrenal inhibition was demonstrated at dosage levels of 5 and 25 mg. of fluorohydrocortisone daily. The substitution of fluorohydrocortisone for cortisone or hydrocortisone in patients receiving long-term corticoid therapy permits the evaluation of adrenal cortical function with standardized corticotropin tests without the necessity for discontinuing effective therapy with adrenal hormones.

Experimental Studies and First Clinical Application of a Colchicinic Derivative With an Antiblastic Action: Trimethylcolchicinic Acid Methyl Ether (Diacethylcolchicine). W. Paolino, G. Pierri and L. Resegotti. Minerva med. **46:**1-12 (Jan. 6) 1955 (In Italian) [Turin, Italy].

After a series of experiments on animals, the authors administered trimethylcolchicinic acid methyl ether (Diacethylcolchicine) intravenously in daily doses of 10 mg. or less to 37 patients with various conditions. After the first injections, five patients with chronic myeloid leukemia experienced a sense of improvement and a gain in appetite. The remission was, however, short and lasted two months at the most. It is assumed that resistance to the drug will ensue after repeated cycles of therapy. At the same time it is suggested that the results may be improved by combining the administration of this substance with irradiation to the spleen in the later period of the therapy. Fifteen patients with malignant lymphogranuloma and three with reticulosarcoma benefited moderately from the drug. Patients in whom these conditions are localized to one area are better treated with radiotherapy while those with diffuse lymphogranuloma are better treated with mustard gas and triethylene melamine (TEM). This colchicine derivative seems to be particularly useful for patients with multiple localizations of either condition in whom the afore-mentioned therapies have failed. The drug was beneficial to five patients with carcinoma of the lung. In one the improvement—clinical as well as radiological—was still present two months after discontinuance of the therapy, and the patient had resumed her job as an office worker. Administration of this substance to patients with cancer of the lung seems justified in the cases in which radical surgical treatment is not possible and provided the patient's condition is not extremely severe and the neoplastic process is not too diffuse. Most of the 37 patients tolerated the therapy well, suggesting that, unlike other antiblastic agents, this colchicinic derivative is not toxic for the organism. The remissions obtained in these patients were almost always of short duration, however. During the therapy the leukocytes' behavior was followed closely, and, as soon as a fall was observed, administration of the drug was discontinued. Signs of impairment to the hemopoietic tissue, such as are frequently found in cases of leukopenia caused by other cytostatic agents, were never observed in these patients. The results obtained indicated that trimethylcolchicinic acid methyl ether has a marked antiblastic activity and is less toxic than colchicine. This is the first report on the use of a colchicine derivative on human beings. More clinical experience is needed.

Clinical and Experimental Studies on Treatment of Tetanus with Periston-N. E. Bickel and J. Dieckhoff. Ztschr. ges. inn. Med. **10:**116-120 (Feb. 1) 1955 (In German) [Leipzig, Germany].

A proprietary 6% solution of polyvinylpyrrolidone (Kollidon) in isotonic sodium chloride solution (Periston-N) was given a therapeutic trial in 14 children between the ages of 6 days and 13 years and in a 52-year-old man with tetanus. On admission all patients were first given 20,000 to 40,000 units of tetanus antitoxin intramuscularly and partly intravenously; they were given repeated tetanus antitoxin injection of 5,000 to 10,000 units for three to four days. Periston-N was given the first time with the first injection of tetanus antitoxin; the single dose consisted of 10 to 15 cc. per kilogram of body weight, which was given daily until the spasms subsided. The total amount of the single dose never exceeded 300 cc. and was administered by slow infusion within 20 to 30 minutes. Undesirable side-effects were not observed. Administration of Periston-N proved effective in 12 of the 15 patients. The spasms subsided rapidly, the generalized rigidity diminished, and all the other manifestations of tetanus receded. In vitro experiments showed that the toxicity of the tetanus toxin can be reduced by Kollidon. Experiments on guinea pigs and rabbits showed that a detoxicating effect can be obtained only by repeated administration of quantitatively adequate doses of Periston-N. Traces of tetanus toxin appeared under the influence of the drug in the urine of several animals that had been given injections of a mixture of Periston-N and 1 lethal mice dose of tetanus toxin, while the renal threshold was found to be near 10 lethal mice doses of tetanus toxin. Because of the rapid lowering of the toxin concentration in the

plasma after the intravenous administration of the toxin, Periston-N, even when it is administered by infusion immediately after the toxin injection, can bind only little toxin in the blood; this finding sugegsts the possibility of a "cell disinfection." One may consider, that Periston-N can dissolve out of the cell the toxin that already had been bound or that Periston-N can render the toxin harmless and thus may cause regression of the manifestations of the disease. Experiments on rabbits showed that best results were obtained with two daily infusions of Kollidon in the amount of 2.5% of body weight until the symptoms of tetanus subsided. Treatment was continued with one daily infusion until objective improvement of the general state was manifested by voracity. The favorable experimental results were confirmed by those obtained in the authors' patients.

Adrenocortical Function During Long-Term Cortisone Therapy: Further Observations. E. W. Fredell, H. P. Johnson, M. A. Krupp and others. A. M. A. Arch. Int. Med. **95**:411-418 (March) 1955 [Chicago].

In 1953 and again in 1954, the response of the adrenal cortex to stimulation with corticotropin was studied in 19 patients with rheumatoid arthritis, scleroderma, Boeck's sarcoid, asthma, and dermatitis, respectively, who had received continuous therapy with cortisone for 13 to 38 months up to 1953 and for 30 to 50 months up to 1954. Drop in circulating eosinophils and rise in 17-ketosteroids and corticoids excreted in the urine were used as criteria for the evaluation of adrenocortical responsiveness. Results showed that function of the adrenal cortex was suppressed by the continuous administration of cortisone but that the adrenal cortex remained responsive to the stimulation with intravenous infusions of corticotropin. It is uncertain whether the degree of suppression was increased as the period of therapy with cortisone was extended. The inability of the suppressed adrenal cortex to respond quickly to corticotropin must be borne in mind constantly in managing patients who are receiving cortisone. In any illness or injury constituting a stress, the need for additional exogenous cortisone must be anticipated. Long-term therapy with cortisone was not shown to produce any characteristic change of thyroid function or serum electrolytes.

A Study of the Action of Tricyclamol Chloride. P. Aylett and A. H. Douthwaite. Brit. M. J. **1**:691-693 (March 19) 1955 [London, England].

The effect of D1-*N*-methyl-3-cyclohexyl-3-hydroxy-3-phenylpropyl pyrrolidinium chloride (tricyclamol chloride) on gastric and duodenal motility and tone and on gastric acidity was tested on four patients with gastric and duodenal ulcers. Animal experiments had shown that tricyclamol chloride, an odorless crystalline substance that is freely soluble in water, has an antispasmodic and parasympatholytic action. The patients were given 25 mg. of tricyclamol chloride intramuscularly 20 minutes before a barium meal and were observed radiologically; comparison was made with barium meals given without the drug. Three patients were given the drug immediately after passing a Ryle tube; two patients were given 50 mg. of the drug intramuscularly and one 50 mg. orally. A test meal was eaten, and gastric contents were taken every 15 minutes. The fourth patient was given 100 mg. of the drug orally half an hour before starting the meal. Two patients received also an alkaline mixture immediately after swallowing the meal. Three patients were given a "standard breakfast" of one boiled egg, two slices of toast, and two cupfuls of tea. The fourth patient received a gruel meal. The drug had a pronounced effect in reducing gastric motility and tone. There was a smaller effect in reducing acidity of the gastric contents after a meal of normal food or gruel. Tricyclamol chloride prolonged the reduction of gastric acidity obtained by a dose of alkali. It is suggested that a combination of 100 mg. of tricyclamol chloride by mouth with a full dose of antacid might go some way toward overcoming the difficulty hitherto experienced in controlling nocturnal secretion in the treatment of duodenal ulcer. Side-effects sufficient to cause slight discomfort were observed in most of the patients in whom the effects of tricyclamol chloride were studied.

PATHOLOGY

Recent Studies on the Diagnosis of Cat Scratch Fever. S. S. Kalter, J. E. Prier and J. T. Prior. Ann. Int. Med. **42**:562-573 (March) 1955 [Lancaster, Pa.].

More than 250 patients with lymphadenopathy of unknown cause were skin-tested with antigen prepared from material obtained from the nodes of several different patients with cat scratch fever. A control group of 94 medical students and laboratory workers was also skin-tested. Of the 250 patients, 210 (84%) had a positive reaction to the test, 15 (6%) a doubtful reaction, and 25 (10%) a negative reaction. Of the 210 positive reactors, 135 (60%) gave a definite history of having been scratched by cats. All 15 doubtful reactors claimed to have been scratched, whereas 5 of the 25 negative reactors had been scratched, 15 had been in contact with cats, and 5 could not recall such a contact. Of the 94 control persons, all but 21 had either been scratched or been in close association with cats for some period. Eighty-three (88.3%) of the 94 control persons had a negative reaction to the skin test, 3 (3.2%) had a positive reaction, and 8 (8.5%) were doubtful reactors. Two of three persons with a positive reaction had been scratched by cats in the past, and six of the doubtful reactors had been scratched. These results suggest that the skin test using an antigen prepared from materials obtained from lymph nodes of patients with cat scratch fever is the best available diagnostic procedure at present. Complement fixation tests were performed with "Lygranum CF" antigen (a proprietary preparation of chick embryo antigen) on 20 single serums obtained from patients late in the course of their disease, two pairs of acute and convalescent serums, and four cat serums. Ten of the 20 single serums had no titer whatsoever, and the remaining 10 had titers varying from 1:5 to 1:160. Of the paired serums, one of the patients from whom they were obtained showed no rise of antibody after about two weeks' illness. The titer with "Lygranum CF" was 1:5 in both instances. The other patient's titer increased from 1:20 to 1:80. All the cats' serums were negative. These cats were domestic pets of patients with cat scratch disease and were clinically normal animals. Thus the serologic findings, although suggestive, can in no way be considered specific. Microscopic studies were made of lymph nodes removed from 30 to 40 patients with proved cat scratch fever. The histopathological findings were nonspecific. In the presence of a history of contact with cats, especially a history of a cat scratch, and a positive skin test, biopsy of an affected enlarged lymph node is not considered essential for the establishment of the diagnosis of cat scratch fever. The cause of the disease remains obscure, as does its relationship to the lymphogranuloma venereum-psittacosis group. Caution in the use of antigenic material for skin testing from patients with a history of jaundice is emphasized.

A Simplied Colorimetric Test for Poliomyelitis Virus and Antibody. M. M. Lipton and A. J. Steigman. Proc. Soc. Exper. Biol. & Med. **88**:114-118 (Jan.) 1955 [Utica, N. Y.].

Lipton and Steigman present a method for the titration of poliomyelitis virus and type-specific antibodies in animal and human serums. The procedure is based on the metabolic activity of viable HeLa cells, which produce acid from glucose, a reaction in which the color of phenol red is changed from red to yellow. In the presence of unneutralized poliomyelitis virus the HeLa cells are destroyed; the medium's color therefore remains unchanged. The advantages of the method include: its technical simplicity, elimination of a monkey colony, and relative ease of perpetual propagation of HeLa cells made into replicable suspensions as needed. Furthermore, the authors observed that even low serum dilutions do not induce toxic changes in the dispersed HeLa cells as compared with the same serums so tested in dispersed monkey kidney cells. This method lends itself to use either for large or small numbers of serum specimens on any given day. An addendum to this report indicates that so far over 2,000 serums have been tested quantitatively against the three types of poliomyelitis virus by the described method.

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QUERIES AND MINOR NOTES

BEER

TO THE EDITOR:—*In a court case in this area a judge ruled that 3.2% beer (by weight) is not intoxicating. What is the opinion of the authorities on this matter?* *M.D., Colorado.*

ANSWER.—Prof. A. J. Carlson and his associates (Studies on Possible Intoxicating Action of 3.2 Per Cent Beer, Chicago, University of Chicago Press, 1934) concluded that beer containing 3.2% alcohol by weight is not intoxicating. This opinion was based on the results of a series of psychological and physical tests as well as on determinations of the percentage of alcohol in the blood of the subjects. Two bottles of beer produced no detectable changes in the subjects and was associated with a concentration of alcohol in the blood of about 0.03%. Four bottles of beer taken on an empty stomach over a period of 30 minutes produced only slight unsteadiness in walking and diminished restraint in speech, the blood alcohol level averaging 0.06%. None of the subjects would have consumed this quantity of beer at this rate at his own motivation. The authors quote Bogen, Widmark, and the British committee as saying that 0.06% is below the figure at which signs of intoxication occur in any considerable number of persons. Greater mental and physical impairment occurred with the forced consumption of larger quantities of beer, and some blood alcohol levels rose as high as 0.13%. This was considered to be below the level at which half of the persons tested in Widmark's statistical studies were found to be under the influence of alcohol. On the other hand, Bjerver and Goldberg (*Quart. J. Stud. Alcohol* **11:**1-30, 1950) point out the difficulties of diagnosing "under the influence," which allow large discrepancies in judgment by different physicians. They determined the effect of alcohol by having their subjects perform actual driving tests involving measurable criteria of performance ability before and after consuming alcohol. The drinking of three or four bottles (1 or 1.3 liters) of 3.2% beer caused a deterioration of from 25 to 30% in performance at alcohol concentrations in the blood between 0.04 and 0.06%. The threshold of impairment in the drivers was found to be between 0.035 and 0.040%. The impairment ratio when the same amount of alcohol was taken in the form of beer and as distilled spirits was as 18:32. Some of the discrepancies between the conclusions of Carlson and those of Bjerver and Goldberg arise from different definitions of "under the influence." If the following definition, paraphrased from an Arizona supreme court decision, were used, much confusion could be avoided: A person is under the influence of alcohol when, owing to the imbibing of alcohol, he has lost to any extent some of that clearness of intellect or self-control that he would otherwise possess. The present opinion is that beer cannot be ruled to be nonintoxicating. It is simply a question of whether enough alcohol has accumulated in the body to cause mental and/or physical deterioration, and this question can be determined by a chemical test for alcohol in body fluids or breath. Also, beer is not on trial. It is the person who has lost some of his self-control and ability by ingesting alcohol that is culpable.

DYES

TO THE EDITOR:—*Please advise me of any toxic effects that may result from splashing methylrosaniline chloride in the eye. I believe this material is used in hectographs and other duplicating machines.* *Everett W. Probst, M.D., Arlington, N. J.*

ANSWER.—A number of dyes almost identical as to chemical structure bear such names as methyl violet, crystal violet, gentian violet, rose aniline, aniline violet, and Pyoktanin. However, there are minor chemical differences. Thus, methylrosaniline chloride is a mixture of hexamethylpararosaniline chloride with, usually, pentamethylpararosaniline chloride and tetramethylpararosaniline chloride. These substances are constituents of hectograph inks, indelible pencils, and therapeutic agents. In most commercial usage these dyes are not used as such but are incorporated into mixtures suitable for specific purposes. The relative harmlessness of this dye group is reflected in the wide application of methylrosaniline in skin affections and its minor use in otology and ophthalmology. Nevertheless, it is widely believed that these dyes in some variations are harmful in connection with surface injuries and that all may be harmful on ingestion in substantial quantity. Thus, it has been reported (Mason, M. L., and Allen, H. S.: *Ann. Surg.* **113:**131, 1941; abstracted in *J. A. M. A.* **116:**1480 [March 29] 1941) that puncture wounds from indelible pencils are far more destructive of tissue than puncture wounds of equal severity from an ordinary lead pencil. Similar is the belief that eye injuries from particles of the indelible lead of pencils are made severer through predilection of the dye for the corneal structure. It is possible that these aggravations of injury are due to other constituents of indelible lead rather than solely to the dye. The same statement may be applied to duplicating machine inks, which again contain constituents other than the dye. Dermatitis from hectograph ink is well known, and yet the same substance in purer form is used in the treatment of dermatitis. All things considered, it appears likely that some members of the group of dyes loosely termed "methyl violet," including methylrosaniline, can be harmful.

TEST FOR COLOR BLINDNESS

TO THE EDITOR:—*Accurate color sense in industrial workers seems to be assuming greater importance with increasing use of color coding of fuels, electric wiring, and other intricate assemblies. What decision should be made about a person who satisfactorily passes the old yarn test, while he fails on several plates of the pseudoisochromatic test book?*

M.D., California.

ANSWER.—Yarn tests such as the Holmgren wool test are today considered unsatisfactory because the procedure is not standardized and because only a small percentage of persons with deficient color perception are detected. Pseudoisochromatic plates such as the Ishihara series are failed by almost all subjects with any degree of red-green color deficiency. For certain industrial tasks in which a moderate degree of defect is not disqualifying, this type of test may, therefore, provide too stringent a criterion. The Farnsworth dichotomous test for color blindness (Psychological Corp., New York City) is failed by about half of the color-deficient group. It is said to be of value in meeting the selection problems of certain industrial jobs.

PREGNANCY TESTS DURING HOT WEATHER

TO THE EDITOR:—*During the heat wave last summer (temperatures in excess of 110 F [43.3 C]), two pregnancy tests at a reliable laboratory gave falsely negative results. The laboratory used Xenopus laevis toads with the patients' serums. Are incorrect tests common during the summer?*

F. C. Katzenstein, M.D., Salem, Ill.

ANSWER.—These toads thrive best at a temperature of 22 C. The temperature of their environment must not be changed rapidly, although they may survive wide fluctuations from 1 C to 33 C if the change is made slowly, so that they become acclimatized. Temperature has little effect on sensitivity, but an increase from 21 C to 31 C decreases the average time between stimulus and response from 18 to 9 hours. Incorrect tests may be commoner during the summer if temperature is not controlled carefully (Landgrebe, F. W., and Samson, L.: *Obst. & Gynaec. Brit. Emp.* **51:**133 [April] 1944).

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

PROCEDURE FOR CATHETERIZATION

To the Editor:—*We are trying to change our procedure for catheterization of the urinary bladder. In the past we cleansed the local area with cotton pledgets dipped in sterile neutral soap and then with pledgets dipped in boric acid solution. Feeling that this method is outmoded, we should like to change to simply a soap-and-water local bath, which would be more in line with the type of preparation that would be given in a home. Some of our physicians advocate simply using soap and water, while some insist on the additional wiping of the area with bichloride of mercury in 1:1,000 dilution or benzalkonium (Zephiran) chloride (aqueous) in 1:1,000 dilution. If Zephiran is used would it affect the urine collected for purposes of culture?* M.D., Connecticut.

Answer.—The best method of cleansing the glans penis or the labia and introitus prior to the insertion of a catheter is by a thorough washing with soap and warm water. This is much better than the conscience-salving use of some so-called cutaneous antiseptic such as bichloride of mercury or benzalkonium. The important thing is to avoid contaminating the end of the catheter by dragging it over the vulva or the anal region prior to its insertion. If benzalkonium is used to sterilize the catheter, it should be washed off with sterile water or normal saline solution before insertion of the catheter for two reasons. 1. In certain patients the urethral and vesical mucous membranes are very intolerant to benzalkonium and marked chemical cystitis and urethritis develop, even though most patients are not sensitive to benzalkonium in a concentration of 1:1,000. 2. If enough benzalkonium is present, it may (theoretically, at least) prevent the growth of bacteria that are present in the urine.

CAFFEINE AND PEPTIC ULCER

To the Editor:—*In patients with peptic ulcer, why is ingestion of caffeine forbidden? Caffeine is a stimulant of the conscious part of the nervous system but is not classed as an autonomic drug. Are other stimulants of the central nervous system, such as strychnine, amphetamine, and ephedrine, likewise proscribed in the presence of ulcers?*

Alfred B. Mason, M.D., Camp Lejeune, N. C.

Answer.—Many stimulants of the central nervous system cause increase of acidity of gastric secretions and increased motility of the stomach. Caffeine is used as a test of neurosecretory responsiveness of gastric function; the efferent pathway is over the vagus nerves. Caffeine is often ingested by patients several times a day and should not be taken between meals or when the stomach is empty. Other similar stimulants are occasionally prescribed for specific needs but, since used less frequently, do less harm in the ulcer patient.

CLEANING FOOTBALL EQUIPMENT

To the Editor:—*Is the usual method of treating material suspected of harboring scabies-producing organisms suitable for the processing of football pants and other equipment without injuring the equipment?*

August J. A. Watzlavick, M.D., Schulenburg, Texas.

Answer.—Despite inquiries made of an equipment keeper, team physicians, dermatologists, professional cleaners and chemists, an absolute answer cannot be given, for the reason that the query is relatively indefinite. For example, football pants used to be made of canvas but are now made of silk, nylon, and wool of widely varying colorings; the jerseys may be made of cotton and wool; and the supporters are partly made of rubber elastic. One method of treating football equipment suspected of harboring scabies is simple dry cleaning. The cleansing system in vogue in some large colleges is simple scrubbing with mild soap flakes and a detergent, using a hand brush.

Dusting before end-of-season storage with dry (nonalkaline) sulfur in the form of finely divided sulfur or flowers of sulfur should be effective without causing fabric injury, with the possible exception of articles partly composed of rubber. In a combination of scrubbing with soap and detergent followed by dry sulfur treatment before storage is used, equipment should be thoroughly rinsed and fully dried before sulfur is applied.

ANESTHESIA AND FULL STOMACH

To the Editor:—*What is the accepted procedure for inducing anesthesia for treatment of trauma when the patient has a full stomach? The response to this question should be guided by the facts that (1) if the patient voluntarily vomits by sticking his finger down his throat, after the conclusion of the induction of anesthesia he still vomits quantities of recently eaten food; (2) if the stomach is washed out with a stomach tube, after administration of the anesthetic he usually vomits quantities of recently eaten food; and (3) when vomiting is induced with emetics, at the conclusion of the operation the patient still vomits quantities of recently eaten food. I know of a patient who died because of aspiration of a large piece of meat after anesthesia was induced for reduction of a fractured arm. Aside from the fact that intubation would have been beneficial if it had been suspected that large pieces of undigested food were present, I doubt if this should be a routine procedure for all persons who have trauma soon after a meal.* M.D., California.

Answer.—Whenever possible a palliative procedure not requiring surgery or anesthesia should be used until the intestinal tract resumes its normal function. Then anesthesia can be initiated without risk. Local or regional block anesthesia should be used whenever possible. If general anesthesia must be used, there are two schools of thought as to whether induction of vomiting by Ewald tube, emetics, finger in the throat, or other means before anesthesia assures safety to the patient. Many anesthetists believe this procedure may increase the hazard by continuing the initiated vomiting reflex and increasing parasympathetic reflexes such as salivation, swallowing, and gagging, so that the parasympathetic responses of laryngeal irritation and gagging are more likely to develop during the induction of anesthesia.

The only safe procedure, when general anesthesia is the anesthetic method of necessity, is to intubate the trachea with the patient under topical anesthesia first and then, when safety from aspiration of vomitus is assured by this means, to induce general anesthesia. There can be no argument against this plan in emergency treatment of extensive trauma, but the attending physician is loath to proceed in this manner when the operation to be done is minor and of short duration. However, the risk of aspiration of vomitus and death is always present, regardless of the extent of the operation. Some anesthetists believe in taking that risk and having the suction, intubation, and bronchoscopic equipment ready so that immediate emergency measures can be instituted should trouble arise.

In young children the induction of anesthesia by the drop ether method is usually considered safe, for the child will vomit during the long induction and will thus empty the stomach. The sympathetic properties of ether further safeguard against the establishment of excess parasympathetic activity after vomiting. To be completely safe, however, intubation should be done on a conscious child and general anesthesia then established. No other method affords complete safety from the hazards of induction of and emergence from anesthesia. Certainly the complications of intubation, such as the occasional broken tooth, although disturbing, cannot compare with the loss of life that may complicate the use of general anesthesia without intubation.

PHENOBARBITAL PROHIBITED IN NURSING MOTHER

To the Editor:—*Please give your opinion on the advisability of an epileptic mother, currently taking 1½ grains (97 mg.) of diphenylhydantoin (Dilantin) sodium and 1½ grains of phenobarbital, both three times daily, nursing by breast her newborn infant.* M.D., New York.

Answer.—Phenobarbital passes from the mother's milk to the nursing infant and acts as a profound sedative to the infant. This happens in the case of other barbiturates as well. Diphenylhydantoin, however, has no effect on the nursing infant. It does gain access to the milk, but it has no adverse effect on the child. If an epileptic mother wishes to nurse, it is advised that she not take phenobarbital.

DOSES DELIVERED IN DIAGNOSTIC RAYING

To the Editor:—*In a tuberculosis hospital many laminagrams (tomographic) films on patients are done. Usually nine exposures: levels, 5 cm. through 13 cm. at 1 cm. differences are done in the anteroposterior view. Frequently three lateral laminagrams are also done. For each exposure, 30 to 100 kvp are used at 36 in. distance between the tube and cassette, and 30 ma. for two seconds, giving 60 ma. seconds for each exposure. What is the exposure level beyond which, for the patient's safety, one should not go? In the literature the amount of roentgens the patient can safely absorb is given, but there is no practical guide or table converting the factors of distance, kilovolt (peak), and milliampere seconds into roentgens. Please advise.* *John A. O'Hale, M.D., Brecksville, Ohio.*

Answer.—It is not surprising that no published tables were found for converting the voltage, current, expesure time, and target-film distance employed in diagnostic raying into dose in roentgens on the surface of a patient's body and at various depths beneath the surface because at least two very important factors are missing from the data, namely, the filtering effect of the tube window and any deliberately added filters and the size of the ports employed. When one wishes to know the doses that are being delivered in diagnostic raying, the usual procedure is to make an actual roentgen meter reading at the surface of the patient's body, measure the so-called half-value layer of the radiation, and then compute the dose at various depths. The making of a particular film will involve rather heavy dosing of skin and superficial tissues when the voltage is low and no added filter is used, whereas high voltage and a 2 to 3 mm. Al filter will greatly reduce the total tissue dose. All else being equal, the tissue dose will be higher for large films and poorly coned beams, smaller when the film is small and the beam closely coned. For the making of 12 laminagrams, it should be possible to arrange voltage, filtration, and coning so that the dose to the skin ranges somewhere between 1.2 and 6.0 r, with the dose at the depth ranging from approximately 0.24 to approximately 1.20 r. These values are small compared with those used in the complete examination of the stomach, including fluoroscopy and films, where the skin dose may range as high as 97 r, and the depth dose 20 r.

PEMPHIGUS

To the Editor:—*My patient has pemphigus. I would like to know the tests used to make a definite diagnosis. What is the latest treatment and final outcome? I have always been taught it was fatal.* *Louise M. Pugliss, M.D., Brooklyn, N. Y.*

Answer.—The diagnosis of pemphigus can be established by histological examination. The characteristic lesion consists of a degeneration of epidermal cells leading to a loss of coherence between the epidermal cells (acantholysis) and thus to the formation of intraepidermal blisters. It is important that only very early blisters be selected for histological examination; otherwise, secondary changes obscure the characteristic changes. There are two major types of pemphigus, pemphigus vulgaris and pemphigus foliaceus. Prior to the advent of corticotropin (ACTH) and cortisone, pemphigus vulgaris nearly always was fatal, while pemphigus foliaceus had a better prognosis, especially in patients under 60 years of age, of whom more than half survived.

The only effective treatment for pemphigus is corticotropin or cortisone. Pemphigus always responds to these agents, but large doses usually are required for the adequate control of the disease. Because large doses have to be administered for long periods of time, side-reactions are common. Therefore, the treatment of pemphigus should be carried out only by someone thoroughly familiar with the disease as well as with the administration of the steroids. Corticotropin or cortisone usually must be given over several years, either continuously or, if possible, in intermittent courses. It seems that after a period of one to several years pemphigus vulgaris and pemphigus foliaceus gradually become inactive and the patient remains well without further treatment. Thus, the steroids appear to be lifesaving drugs in pemphigus. The greatest danger to the life of the patient nowadays lies in possibly fatal complications to the therapy with corticotropin or cortisone.

SURGICAL CLOSURE OF PERITONEUM

To the Editor:—*Could you give the consensus of surgical policy on the following points in closure of the peritoneum, fascia, and skin after (1) intestinal resection and (2) gastrectomy? 1. Instruments, towels, and gloves that were used on the intestine are never used for the abdominal closure. 2. Instruments used for the resection of malignant tissue are never reused for normal, healthy tissue.*

Louis Salerno, M.D., Passaic, N. J.

Answer.—In preparation for an intestinal resection or gastrectomy, the draping about the wound is covered with additional towels and packs. These extra protectors and all instruments used during the gastrointestinal work are discarded when the open part of the resection is finished. Gloves are washed with a solution of mercury bichloride, new towels and packs placed about the wound, and the operation finished. For the resection of malignant tissue, the same procedure is carried out. In every way contamination with malignant cells should be prevented so as to minimize their spread or implantation into normal healthy tissue. Once protective measures are set up and thoroughly understood by the staff, the carrying out of these procedures becomes an easy routine without fuss or loss of time.

METABOLISM OF GLYCERIN

To the Editor:—*Is glycerin absorbed from the intestine of man, and, if so, what is its caloric value? If absorbed and metabolized, how is the glycerin handled—as a carbohydrate or a fat? Can patients on low-fat diets ingest products containing glycerin with impunity?* *M.D., New York.*

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—Glycerin is absorbed and metabolized by man. After absorption it is converted to glucose and is used as such. Weight for weight, it has roughly the same caloric value as glucose. There is, therefore, no apparent reason why patients on low-fat diets should not eat appropriate amounts of products containing it. Glycerin split off in the digestion of fat, or in the metabolism of endogenous neutral fat, presumably follows the same pathway as ingested glycerin. However, it should be pointed out that whether the glycerin or the resulting glucose is degraded to carbon dioxide and water or whether it is used to reconstitute body fat depends on the total calories consumed. Whenever the total calories ingested exceed the total energy expenditure, glucose from any source (or perhaps the glycerin without conversion to glucose) may be used in the formation of body fat.

Answer.—Glycerin, chemically known as glycerol, is readily absorbed, as such, from the intestine. Fat contains glycerin that is liberated as the fat breaks down stepwise in the process of digestion and absorption. Glycerin, in either case, is metabolized like a carbohydrate. Its normal structure is much like that of dextrose; its caloric value gram for gram is about the same as that of dextrose, 4 calories per gram. Like dextrose, also, it is either oxidized to carbondioxide and water or converted to fat. The ingestion of glycerin should not increase the level of blood fat, and thus the use of glycerin would not be contraindicated when low-fat diets are prescribed in an effort to combat arteriosclerosis. If, however, restriction of fat is designed to effect reduction of body weight, the calories from glycerin, if much is used, should receive consideration. The use of glycerin in diabetes as a sweetening agent is not advantageous because its use in severe diabetes is no more satisfactory than that of sugar.

CALCIFIED PLAQUE IN AORTA

To the Editor:—*What significance have sclerotic plaques in the abdominal aorta in regard to life expectancy or as a herald of more serious complications in a man aged 56?*

M.D., Michigan.

Answer.—The roentgen ray findings of a calcified plaque in the aorta do not tell anything about an impaired circulation through that vessel; in fact, it takes about 70% of reduction in the lumen of the vessel before an arterial stenosis becomes manifest.

INJECTION OF ALCOHOL IN SPINAL CANAL

To the Editor:—*Please send me the technique for injection of alcohol into the spinal canal for relief of intractable pain due to carcinoma of the prostate with metastasis to the vertebra.*

Lewis Brings, M.D., Cumberland, Md.

Answer.—The principle involved in the injection of alcohol into the subarachnoid space for the relief of pain is the destruction by the alcohol of pain-bearing afferent fibers. One must clearly recognize, however, that the alcohol serves as a two-edged sword and that destruction of efferent fibers or of spinal cord rather than peripheral nerve elements may be caused. Since absolute alcohol is lighter than spinal fluid, it may be employed as a flotation medium. The patient should be placed in the horizontal position, with the root fibers to be blocked on the uppermost side. Turning the patient slightly forward probably increases the likelihood of the maximum concentration of alcohol occurring about the posterior rather than the ventral roots. If the sacral roots are to be bathed in alcohol the hips may well be slightly elevated. If, on the other hand, the mid-lumbar roots are to be interrupted, a folded sheet placed at the iliac crest helps to place the foramens of exits of these nerve roots at the highest level. Lumbar puncture is then carried out in the standard fashion (or the puncture may be done before the final positioning of the patient) and then 1 cc. of absolute alcohol is slowly injected over the course of one minute. It is common practice to keep the patient in this position for the next half hour, since how quickly the alcohol fixes is an unknown factor. A check of sensory loss at this time may show satisfactory block. If not, an additional 1 cc. may again be injected over a period of one minute. At least one case of monoplegia has resulted from the indiscreet use of alcohol injected into the subarachnoid space.

The technique has no indications in carcinoma of the prostate. A number of endocrine methods of control are of high value in prostatic cancer, and irradiation of the spine with roentgen rays often relieves intractable pain.

BACTERIOLOGICAL PROCEDURES

To the Editor:—*In areas where laboratory services are not offered the greatest need is for bacteriological procedures. In cases of throat cultures for streptococci, clinical appearance, history, and white blood cell count can leave one in doubt. In such cases it would help if prepared mediums could be used. Would simple throat-swab streaking of blood agar slants give sufficient information? Along these same lines, where Streptococcus infection is suspected, an elevated white blood cell count is of value. Is an increase in the percentage of polymorphonuclear leukocytes of even more significance? Might one have a normal or only slightly elevated total white blood cell count but have a marked predominance of polymorphonuclear leukocytes and thereby support a diagnosis of Streptococcus infection?*

M.D., Indiana.

Answer.—Swab streaking of blood agar slants for transmittal to a laboratory by mail cannot be used routinely. Colony formation on a slant cannot be differentiated unless an almost pure culture of the organism is obtained, although some hemolytic colonies may develop at the upper portion of the slant where the medium is thin. This latter, however, cannot be relied on. The medium itself presents a problem. Blood agar will hemolyze when kept over a period of time. Usually it must be used within about two weeks. Loeffler's serum slants can be prepared and mailed with some success. After being incubated at 37 C for 18 to 24 hours, a red blood agar plate is prepared from the slant. After further incubation this plate may then be examined for hemolytic organisms. Some laboratories request the physician to prepare swabs and to mail the swab directly to the laboratory. With such a procedure, however, results cannot be guaranteed, since the organism may be killed by drying. A high white blood cell count is not specific in Streptococcus infections. If the patient's resistance is high, a high polymorphonuclear count may be found. If the patient's resistance is low, a low polymorphonuclear count may be found.

TONSILLECTOMY

To the Editor:—*A 5-year-old boy was being given anesthetic for a tonsillectomy. There were no apparent cardiac or pulmonary defects, and the tonsils were not unduly enlarged. Induction was begun with ethyl chloride and then the anesthetist switched to ether. Several times before sufficient relaxation was achieved the patient stopped breathing and became cyanotic, without any apparent laryngeal spasm. As soon as administration of the anesthetic was stopped, or within a few seconds thereafter, the child would begin to breathe again and his color would return to normal. There was not sufficient relaxation to put in an artificial airway, but the tongue did not seem to be causing any obstruction. Preoperative preparation consisted of atropine sulfate 1/300 grain (0.20 mg.) and codeine ½ grain (30 mg.) both given intramuscularly about 30 minutes prior to beginning administration of the anesthetic. Please comment on the causes for the difficult induction and repeated episodes of cyanosis without spasm or relaxation in this case, also on the use of codeine as preoperative medication. Would 30 mg. of Demerol given intramuscularly be preferable or satisfactory in this case? In switching from ethyl chloride to ether anesthesia, is it necessary or advisable to change masks, and if so, why? While it is not a factor in this case, what is the prevailing opinion as to how long one should wait after an attack of acute tonsillitis before performing a tonsillectomy, especially when the attack of tonsillitis was treated by massive doses of antibiotics? Do most otolaryngologists recommend routine use of antibiotics preoperatively or postoperatively, or both, in uncomplicated cases?*

M.D., Ohio.

Answer.—This episode might have been due to breath holding to the point of cyanosis because of too great a preliminary concentration of the anesthetic. This is the less likely of a number of explanations, because there was no laryngospasm. Another possibility is this: ethyl chloride is a potent agent; forcing it allows one to arrive at a deep stage of anesthesia in seconds, and the patient may stop breathing; withdrawing the mask allows the ethyl chloride to be rapidly expelled and the patient quickly wakes up. Ethyl chloride is preferably given with oxygen (insufflated under the mask) by the drop method, and for induction only. There is no need to switch masks on changing to ether. The preanesthetic medication was not a likely factor in the happenings described, and either of the choices is acceptable. The length of time one should wait before operating, after an attack of acute tonsillitis varies. It depends on the severity of the preceding attack and whether the patient has returned to, what for him would be, a normal state of health. This would be easiest to judge after a single attack, but where, as frequently happens there is a series of flareups with relatively little time in between, it may be necessary to intervene by operation before the patient has had time to be himself. Even when the patient is treated with large doses of antibiotics the length of time these are given is more important at times than the dosage. The masking effect of the antibiotics is well known, and important symptoms like temperature may quickly disappear under their use, but the patient must still be given time to recover his strength. It is in these instances that preparation for some time previously by antibiotics is often desirable. As to the routine use of antibiotics pre and postoperatively in uncomplicated cases, the impression of many is that this is not desirable. The healthy adult and child in good physical condition may approach this operation with every reason to believe that recovery will take place normally.

CANCER OF TONGUE

To the Editor:—*If a patient has carcinoma of the tongue or tonsil region, can he get cancer of the stomach from swallowing detached cancer cells?*

Joseph J. Lordi, M.D., New York.

Answer.—There is no evidence that a patient can get cancer of the stomach or any other part of the intestinal tract from swallowing detached cancer cells. From a primary in the tract or tonsillar region, it is presumed that such cells are properly digested by the gastric and intestinal secretions.

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A RELATIVELY NEW MUSCLE RELAXANT

To the Editor:—*When used properly is anectine a relatively safe drug as an adjunct for thiopental and other forms of general anesthesia? Has it been known to cause prolonged postoperative hypotension?*

M.D., Kentucky.

Answer.—Anectine is a relatively new and interesting muscle relaxant. It has not yet been studied extensively enough nor has it been used widely enough in the clinic to justify dogmatic statements concerning it. In an extensive study of nearly 600,000 anesthesias carried out in 10 university hospitals (Beecher, H. K., and Todd, D. P.: A Study of the Deaths Associated with Anesthesia and Surgery, *Ann. Surg.* **140:**2-34, 1954) it was found there was a disturbingly high incidence of deaths characterized as anesthesia deaths in the 10 participating hospitals when muscle relaxants entered the picture. This very much higher incidence held during induction of anesthesia, that is, before complications of surgery might have influenced the situation. The data of that study did not contain enough cases in which anectine (succinylcholine) was used to make it possible to tell whether this new agent would have the same worrisome increase in anesthesia deaths as was associated with the other agents or not. Further time and study will be necessary before the relative safety of this new agent can be determined. A new observation concerning the muscle relaxants that they studied was that disasters with the use of these agents are likely to be associated with circulatory impairment as well as respiratory difficulties. Circulatory collapse occurred notwithstanding prompt and satisfactory artificial respiration in a number of cases. It is not yet known whether this will be the case with anectine or not. Past experience indicates that it will be well to keep a watchful eye on circulatory matters as, for example, prolonged hypotension.

RETINOCHOROIDITIS

To the Editor:—*A patient gave a history of dust having flown into the right eye. The following day the eye became red and irritable. The plant physician prescribed eye drops and advised the patient to see a specialist. Two days following the accident he was seen by an ophthalmologist. There was marked conjunctival injection, and the eye was painful. The vision became blurred, and the media became cloudy. A severe chorioretinitis and uveitis developed, and the patient was hospitalized and thoroughly investigated. Sixteen days prior to the accident, the patient had had a routine examination for glasses by an ophthalmologist. The latter reported no evidence of any ocular abnormality at the time of his examination except a slight refractive error; the visual acuity was readily corrected to 20/20. The findings have been confirmed by several ophthalmologists. I would like your opinion on whether the original injury could be responsible for the onset of the uveitis and whether this case should, therefore, be considered compensable under the workmen's compensation law.*

M.D., New York.

Answer.—Dust in an eye cannot cause a retinochoroiditis. In this case the patient had a congestion of the eyeball and incorrectly ascribed it to dust. As the deep ocular infection progressed, the injection increased and was accompanied by pain and blurred vision, a typical uveitis. The clouding of the media was from the combination of the aqueous and vitreous opacities; the pain was from the anterior uveal involvement, an iritis; and the decreased vision was from the posterior fundus focus, a retinochoroiditis. The alleged dust in the eye neither caused nor influenced the uveitis. The patient is, therefore, not entitled to compensation under the workmen's compensation act.

CALCIFICATION OF COSTAL CARTILAGES

To the Editor:—*In several young people, one 16 years old, the costal cartilages are extensively calcified on x-ray films. Is such a degenerative process significant in young people?*

Robert E. Casey, M.D., Texas City, Texas.

Answer.—Calcification of the costal cartilages in young people is not uncommon and is not of clinical importance.

ANOSMIA

To the Editor:—*A woman 68 years of age suffered an electric shock 18 months ago. She did not lose consciousness but felt "shaken up" and for the next three months became tired easily. Soon after the shock she noted loss of sense of smell, and anosmia is now complete. Examination of the nose, throat, and sinuses revealed no other abnormality. Is it likely that the shock caused the anosmia?*

John G. Wilcox, M.D., Santa Ana, Calif.

Answer.—Although it is possible that a severe electric shock might produce an anosmia, it is unlikely. To give an unqualified answer to this question one would have to have had the record of a neurological examination carried out prior to the shock and a similarly complete examination performed at some time after the traumatic episode. Many individuals, especially the older age group, have lost the sense of smell without being aware of it. In the absence of any abnormal nose, throat, and sinus findings at this time, and in the absence of other abnormal neurological findings other than the loss of the sense of smell, one would have to conclude that the electric shock probably was not responsible for the anosmia.

LUMBAR SYMPATHECTOMY FOR PERIPHERAL VASCULAR DISEASE

To the Editor:—*Please give information on the value of lumbar sympathectomy in peripheral vascular disease of the lower extremity, particularly arteriosclerotic gangrene.*

John J. Bedrick, M.D., Bayonne, N. J.

Answer.—Lumbar sympathectomy produces vasomotor paralysis in the lower extremity, thereby eliminating fluctuations of blood flow that occur in the erect position on exposure of the rest of the body to cold and as a result of emotional stress. Thus, the diminished blood flow encountered in peripheral vascular disease can be utilized for the metabolic needs of the tissues and will not serve postural reflexes or heat regulation. The skin of the extremity in which sympathectomy has been done is dry and there is no loss of heat by evaporation; nor can a fungus often present in cases of impaired peripheral blood flow thrive in the absence of moisture. The increase in blood flow is surely present for the skin, but the increase in muscle flow is usually insufficient to improve claudication; to obtain significant relief from claudication the patency of the main vessel has to be restored by endarterectomy or vessel graft, but these procedures are only feasible above the level of the popliteal space. In arteriosclerotic gangrene, where amputation is almost inevitable unless a small patch of skin is involved, sympathectomy may lower the level of amputation, but each case has to be individually evaluated. It is often true that the opposite, nongangrenous extremity is the one that is more apt to benefit from lumbar sympathectomy, since it protects the vulnerable skin of the remaining limb from an early breakdown.

NASAL CONGESTION DURING PREGNANCY

To the Editor:—*Is there any treatment for the nasal congestion that occasionally develops in pregnant women? A patient of mine, herself a physician, has been greatly troubled by completely blocked nares since the third month of pregnancy. There is no history or physical evidence of allergy. The sinuses are clear. The nasal mucosa is tremendously swollen and beefy red in color. The nasal septum is in the midline. There is a small amount of mucoid discharge. Various antihistaminic drugs and the whole gamut of vasoconstricting nose drops have given no relief. A plastic tube run through the inferior meatus gives slight relief. Under consideration is the submucous injection of a sclerosing solution or electrocauterization of the mucosa of the turbinates.*

Alan Davidson, M.D., New Bern, N. C.

Answer.—In view of the fact that nasal congestion during pregnancy is not a serious condition, there is no need for special therapy. Only mild medicaments such as menthol ointment should be used. After delivery the nasal congestion will disappear.

CRAMPS AND EDEMA IN LEGS

To the Editor:—*A man, 74 years old, mildly diabetic, but not on a strict diet or taking insulin, stopped smoking three years ago when intermittent claudication started. His blood pressure was always below 140 mm. Hg; sometimes albumin had been found on urinalysis for many years but never casts. Cancer of the prostate was suspected, but no clinical symptoms were found. The patient took diethylstilbestrol, 1 grain (60 mg.) four times a day, for six months, then 1 capsule of Tace twice a day. He has had edema for a year in both legs, sometimes up to the knees, not much influenced by walking. Nearly every night he awakens with painful cramps in both legs, which seem to come on as soon as one of his feet makes a dorsiflexion. Are the cramps aggravated by Tace or stilbestrol? His weight has increased 5 lb. (2.3 kg.) in six months. Last February he had a mild coronary attack, which showed on the electrocardiogram. For the cramps he has tried quinine, benadryl, and papaverine. Could the edema be of dystrophic nature?*

M.D., Ohio.

Answer.—It is likely that the edema of both legs is partly due to the estrogens he is taking as well as some cardiac deficiency. The intermittent claudication may be due to the arteriosclerosis associated with his diabetes. It is unlikely that the cramps are aggravated by the estrogens. Cramps are often precipitated by overbreathing during sleep, and rebreathing by covering one's head sometimes gives some comfort. Raising the head of the bed also deserves a trial.

BARBITURATES IN URINE

To the Editor:—*Please give instructions for detecting barbiturates in urine. The method of Green, Veitch, and Koppanyi is of particular interest.*

Connell H. Miller, M.D., Sligo, Pa.

Answer.—The method recommended for the qualitative determination of barbiturate in urine is as follows (Gradwohl, R. B. H.: Legal Medicine, St. Louis, C. V. Mosby Company, 1954, p. 640): Directly to 100 cc. of urine that has been acidified with a few drops of dilute sulfuric acid, add twice the quantity of ether and shake in a separatory funnel. Allow to settle, filter ether layer through filter paper, and carefully evaporate to dryness on water bath. The residue may have slight color; if so, redissolve residue with dilute sodium hydroxide 0.5 N (15 cc.), filter, and just barely acidify with dilute sulfuric acid and again extract with ether. Repeat as above and again obtain residue. Residue is now dissolved with 1 cc. of chloroform. Several drops are transferred to a microtest tube, then 2 drops of cobalt acetate (1% in absolute methyl alcohol) are added. Mix and then stratify with 5 drops of isopropyl amine (5% in absolute methyl alcohol). A violet interface indicates the presence of barbiturates. Moisture or water may interfere with this reaction. Ureides, Bromural, hydantoin, theophylline, and theobromine also give positive results. The procedure of Green, Veitch, and Koppanyi is similar except that they recommend the addition of 5 gm. of Lloyd's reagent (a purified siliceous earth) per 100 ml. of urine to the acid urine to remove highly pigmented material. The filtrate is then extracted with ether as above.

HYPOTHYROIDISM FOLLOWING PREGNANCY

To the Editor:—*What explanation can be given for hypothyroidism following the postpartum period of pregnancy? A 38-year-old obese white woman progressed through her first pregnancy without complaints associated with hypothyroidism. After the puerperium, she had swelling of the face, hands, extremities, and abdomen. The pulse rate was slowed, with dulling of mental activity, sluggishness of movement, constipation, and abdominal fulness with discomfort. Treatment with thyroid brought about complete remission of complaints. These same findings and complaints followed her second pregnancy. There is history of hypothyroidism in her family.*

Joseph V. Waitkunas, M.D., Woodhull, Ill.

Answer.—Postpartum hypothyroidism is extremely rare. A possible explanation is that during pregnancy the pituitary output is diminished, and it may happen that there is a lag in the resumption of normal pituitary activity.

MASTER AND NYLIN TESTS

To the Editor:—***1. What is a false-positive Master test? 2. What does it mean if a patient has a positive two-step Master test without cardiac or other symptoms? 3. What is the Nylin effort test? 4. What is the difference between the Nylin test and the Master test? 5. Which of the two tests gives more information?***

Aaron M. Gorelik, M.D., Bronx, N. Y.

Answer.—In the first question, "false" is a poor term, but the test can show RS-T depressions and/or T-wave inversions in normal people or in people who are excitable. Therefore, a "positive" test should never be interpreted by itself but rather in conjunction with the clinical story and clinical findings. To answer the second question, it can be said that the results of the test should be disregarded if the patient has no cardiac symptoms or signs. In regard to the third question, Gustav Nylin in 1933 described the test of heart function in Clinical Tests of Function of the Heart (*Acta med. scandinav.*, supp. 52, pp. 1-92, 1933) and again More Recent Developments of Heart Function Tests (*J. A. M. A.* **109**:1333-1337 [Oct. 23] 1937). It has a specially constructed stairway, one meter high, in which the patient must walk a certain number of rounds, the rate determined by a "metronome." He uses the oxygen consumption of the fasting subject at rest and then that between the second and fifth minutes after cessation of a definite amount of work. The increase of oxygen is noted, but there is no attempt to evaluate or standardize electrocardiographic changes. This consultant has had no experience with it and therefore is not in a position to say how it compares with the two-step test. Of course, in Nylin's laboratory the 10% anoxemia test has been used a good deal, particularly by his associate Bjorck.

URTICARIA FOLLOWING PARASITIC INFESTATION

To the Editor:—*Has Endolimax nana ever been incriminated as the cause of massive urticaria? A patient who has recurrent urticaria has been thoroughly examined, and nothing else was found.*

Robert E. Sandlin, M.D., Antioch, Calif.

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—Endolimax nana has never been incriminated as the cause of any pathological condition. It is a very common commensal inhabitant of the lumen of the colon in man. There would be no more justification in assuming that recurrent urticaria is due to this ameba than in assuming that the urticaria is due to any one of the normal intestinal bacteria.

Answer.—Allergic manifestations or cutaneous reactivity, or both, have been found to be caused by infestations by a number of parasites, such as tapeworms, Ascaris, Trichinella, Schistosoma, Oxyuris, Strongyloids, and Filavia. Allergic manifestations have also been claimed to result from such protozoa as malarial organisms. It is likely that other protozoan parasites such as amebas, Giardia lamblia, and trichomonads may produce allergic manifestations. Although reports of allergy to Endolimax nana are not known, it is within the bounds of probability that such allergy may exist. Insufficient attention has been given to the entire subject of allergy to animal parasites.

LOSS OF EYELASHES

To the Editor:—*At the age of 7 a patient lost all her eyelashes for one month. Since then she has had frequent episodes of losing all eyelashes in both eyes. Recently she lost them again, but with the birth of a boy, now a month old, she feels they are coming back. Is there any treatment for this?*

M.D., California.

Answer.—The description suggests the diagnosis of alopecia areata, the cause of which is obscure. Psychoneurotic influences seem to be of importance in most cases, but instances of association with refractive errors and cranial trauma have also been recorded. When it involves the scalp, stimulation-type therapy seems to help. More often than not, the hairs regrow spontaneously.

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